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University of Khartoum
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Brain Tumors among Sudanese Patients

(A histopathological Study)

By

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Dedication

To soul of my father.

To my mother.

To my lovely husband and Kids

Acknowledgements

Thanks to God for blessing me and giving me strength to complete this study.

Thanks and appreciation to Dr. Ahmed I. Shumoo for his valuable instruction and guidance during his supervision of this study. Gratitude also extends to my co-supervisor Dr. Lemyaa A.M. Elhassan for her valuable instructions.

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ABSTRACT

Background: Brain tumor incidence rates increased over the past several decades in most developed countries, particularly in the elderly.

Design: This is a descriptive retrospective study carried out in the period from January 1st 2009 to April 1st 2010.

Settings: The study was conducted in two laboratories, the National Health Laboratory (NHL) and Alzahrawi Private Laboratory (Khartoum).

Objectives: To study the histopathological pattern of brain tumors in Sudan.

Methods: Data were collected from patient's request forms in a predesigned questionnaire. All the histopathological slides of the study were retrieved and reviewed by the investigator with the help and supervision of experienced Histopathologists to confirm diagnosis, determine the histopathological types and classify the tumor using WHO grading system (2007).Ninety cases fulfilled the criteria of the questionnaire. The data were electronically processed and analyzed by computer using Statistical Package for Social Sciences (SPSS) software.

Results: Revision of the cases were consistent with the previous diagnosis (100%).The age of patients ranged from 2 to 80 years, the commonest age group was from 40 to 50 years (23.1%). Male constituted (58.8%). Meningioma was the most common brain tumor constituting (53.3%) of all brain tumors. Astrocytoma

came next (17.7%), pituitary adenoma (8.8%), craniopharyngioma (6.6%), ependymoma (4.4%), oligodendroglioma (3.3%), medulloblastoma (3.3%), epidermoid cyst (1.1%), and undiagnosed (1.1%).WHO grade (I) meningiorna was 87.6% ,grade (II) 8.3%,grade (III) 4.2%.WHO grade (I) astrocytorna was (62.1%), grade (III) 6.2%, grade (IV) 31.2%. Regarding the histological sub types of meningioma, the most common sub type was transitional type (4 1%) , this was followed by meningothelial (35.4%), atypical (8.3%), fibrous (6.3%), Psarnrnomatous (4.2%) and anaplastic (4.2%).The most common histological subastrocytoma was pilocytic astrocytoma (62.1%),this was followed by glioblastorna (31.2%) and fibrilary (6.2%). Cerebral hemispheres were the most common anatomical sites (53.5%),this was followed by cerebellar hemispheres (l2.2%),pituitary gland (8.8%) olfactory groove (5.5%) and orbital (3.3%),other sites (13.7%).

Conclusions: The study concluded that, the results were consistent with those revealed by WHO study.

المستخلص

خلفية: لقد ازداد معدل الحالات المسجلة من ورم المخ خلال العقود الأخيرة في البلدان المتقدمة خاصة لدى كبار السن.

التصميم: هذه دراسة وصفية رجعية، تم إجراؤها في الفترة من الأول من يناير 2009م وحتى الأول من أبريل 2010م.

الإعدادات: تم إجراء هذه الدراسة في معملين للأنسجة هما: المعمل القومي الصحي ومختبر الزهراوي الخاص (الخرطوم).

الأهداف: تهدف إلى دراسة النمط النسيجي المرضي لأورام المخ في السودان.

الطريقة: تم جمع البيانات من استمارة المرضى ووضعها في استبيان معد مسبقاً. تم إعادة واستعراض كل الشرائح النسيج-مرضية بمساعدة وإشراف أخصائي أمراض النسيج لتأكيد التشخيص، كما تم تحديد نوع المرض النسيجي وتصنيف الأورام باستخدام نظام تصنييف منظمة الصحة العالمية (2007م). تم جمع 110 حالة، فيما تم إبعاد 20 حالة لعدم اكتمال بياناتها. أُستخدم الكمبيوتر لتحليل البيانات من خلال برنامج الحزمة الإحصائية للعلوم الاجتماعية.

النتائج: كانت مراجعة الحالات متوافقة مع التشخيص السابق (100%)، أعمار المرضى تراوح ما بين سنتين إلى 80 سنة، والفئة العمرية الأكثر شيوعاً 45 إلى 50 سنة (23.1%)، الذكور مثلوا 58.8%. أورام الأغشية السحائية كان الأكثر شيوعاً حيث مثل 53.3% من مجموع الأورام، ثم تلتها أورام النجيمات (17.7%)، ورم الغدة النخامية (8.8%)، الورم القحفي البلعومي (6.6%)، ورم البطانة العصبية (4.4%)، الورم الدبقي قليل التغصن والورم الأرومي النخاعي مثلوا (3.3%) لكلٍ، ورم الكيس

البشراني، والأورام الغير معروفة (1.1%) لكلٍ. ورم الغشاء السحائي من الدرجة الأولى حسب تصنيف منظمة الصحة العالمية مثل 87.6%، ومن الدرجة الثانية كان 8.3%، ومن الدرجة الثالثة كان 4.2%. أورام النجيمات من الدرجة الأولى حسب تصنيف منظمة الصحة العالمية مثلت 62.1%، ومن الدرجة الثانية كان 6.2%، ومن الدرجة الثالثة كان 31.2%. فيما يخص الأنواع الفرعية لأورام الغشاء السحائي فأكثرها شيوعاً هو النوع الانتقالي 41%، ثم تبعتها أورام طبقات الخلايا السحائية حيث مثلت 35.4%، الورم الشاذ (غير نموذجي) مثل 8.3%، ورم الأنسجة الليفية مثل 6.3%، الورم الرملي كان 4.2%، الورم الكشمي 4.2%. فيما يخص أنواع الفرعية لأورام النجيمات فإن أكثرها شيوعاً كان ورم النجيمات شعرية الخلايا حيث مثلت 62.1%، ثم تلاها الورم الأرومي الدبقي 31.2%، ثم ورم النجيمات الليفية حيث مثل 6.2%. المخ كان أكثر المواقع التشريحية حيث مثل 53.5% ثم تبعها فوق السرجي 15.5%، ثم المخيخ 12.2%، التجويف الشمي 5.5% ثم المحجري حيث مثل 3.3%.

الخلاصة: خلصت الدراسة إلى أن النتائج المُتحصل عليها متوافقة مع ما جاء في دراسات منظمة الصحة العالمية ومع الدراسات السابقة في السودان.

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Declaration

Hereby, I declare that, the data and results provided in this study are of my own efforts and conducted specially for this study.

INTRODUCTION

Brain and other central nervous system (CNS) tumours include a variety of histopathologic subtypes, but the most common, by far, are gliomas. These tumors, which arise from the glial cells that surround and support neurons, include astrocytoma, glioblastoma, oligodendroglioma, oligoastrocytoma, and ependymoma.[1]

Medulloblastoma, another neuroepithelial cancer, is relatively common in children but rare in adults. Brain tumourin children typically arise in the cerebellum, whereas brain tumour in adults are more likely to occur in the cerebral hemispheres.[1] In adults, older age at diagnosis of brain tumour is associated with higher tumor grade and poorer prognosis. Indeed, glioblastoma is among the most lethal of all tumours. Molecular studies of brain tumours reveal still greater heterogeneity of tumor types than is apparent based on histopathology, and efforts are underway to develop a molecular classification of brain tumour.[1]

Very little is known about the etiology of brain and other CNS tumours. These tumours occur in association with several rare familial cancer syndromes, such as neurofibromatosis type 1 and Li-Fraumeni syndrome, but genetic predisposition related to such syndromes is unlikely to account for more than a few percent of brain tumours. The only clearly established environmental risk factor is ionizing radiation, particularly for exposures to therapeutic doses during childhood. Risks

related to modern diagnostic radiography probably are very small. Unlike ionizing radiation, there is little evidence that non-ionizing radiation from electric power lines, appliances, or cellular telephones causes brain or other CNS cancers.[1]

Recorded brain tumour incidence rates increased over the past several decades in most developed countries, particularly in the elderly, but this is generally thought to be due more to improved diagnosis than to a real increase in incidence. Incidence of glioma is positively associated with socioeconomic status. In the United States, incidence is highest in Whites, intermediate for Blacks, and lowest for Asians; however, incidence rates for brain tumour exhibit less international variation than do most tumours, particularly when probable differences in completeness of diagnosis are taken into account. tumourof the brain and other CNS are more common in males than females. A possible role of steroid sex hormones has been hypothesized, and a recent report noted reduced risk of glioma associated with early age at menarche and early age at first live birth.[64] Several studies have indicated a reduced risk of glioma among persons with a history of allergies or certain infections, possibly indicating a role for immune factors.[65,66] A recent report noted an inverse association between use of nonsteroidal anti-inflammatory drugs and glioblastoma.[67] The blood-brain barrier is effective at keeping many potentially toxic agents in the bloodstream from reaching the glial cells

that give rise to most brain tumours. In studies with experimental animals,[68,69])The most potent known chemical neurocarcinogens are nitrosamides, such as nitrosoureas, which can cross the blood brain barrier. Such compounds can be formed in the stomach from nitrites and amides in the diet. Whether they are important carcinogens in humans is an unresolved issue. Experimental studies indicate that the developing nervous system is more susceptible to carcinogens than is the mature nervous system. The suggestion of a higher radiation-related brain tumour risk for children compared with adults is consistent with this observation.[1]

LITERATURE REVIEW

Normal anatomy:

The CNS consists of the cerebrum, brain stem, cerebellum and spinal cord. It has virtually no connective tissue and is therefore, a relatively soft, gel-like organ. The brain may be broadly but usefully divided into supra tentorial and infra tentorial components (tentorium cerebelli). The infra tentorial structure are collectively designated the posterior fossa elements (the cerebellum and most of the brain stem including the pons and medulla). The supra tentorial CNS consist of cerebrum (subdivided into frontal, parietal, temporal and occipital lobes) and deep nuclei of the basal ganglia, thalamus and hypothalamus. Within the CNS, the connective tissue is scant and essentially restricted to the adventitia of blood vessels. There are no resident lymphoid elements.

Embryology:

Neural tissues develop from embryonic ectoderm that is induced to differentiate by the underlying notochord. First, a neural plate forms; then the edges of the plate thicken, forming the neural groove. The edges of the groove grow toward each other and unlimitely fuse, forming the neural tube. This structure gives rise to the entire central nervous system, including neurons, glial cells, ependymal cells, and the epithelial cells of the choroid plexus.[(2)]

Cells lateral to the neural groove form the neural crest. These cells migrate and give rise to most of the peripheral nervous system, as well as a number of other a lot of structures. Neural crest derivatives include (1) chromaffin cells of the adrenal medulla (2) melanocytes of skin and subcutaneous tissues (3) odontoblasts (4) cells of the pia mater and the arachnoid; (5) sensory neurons of cranial and spinal sensory ganglia; (6) postganglionic neurons or sympathetic and parasympathetic ganglia; (7) Schwann cells of peripheral axons; and (8) satellite cells of peripheral ganglia.[2]

Histology:

The principal cells of the CNS are:[2] neurons, glial cells, cells that compose the meninges and blood vessels.

1- Neurons vary considerably in structure and size throughout the nervous system and within a given brain region. Immunohistochemical markers for neurons and their processes, commonly used in diagnostic work include neurofilament protein, Neu N and synaptophysin.

2- Glial cells are derived from neuroectoderm (macroglia) astrocytes ,oligodendrocystes- ependyma) or from the bone marrow (Microglia). Glial cells have important structural and metabolic interaction with neurons and their dendritic and axonal processes; they also have a primary role in wide range of functions and reaction to injury

including inflammation, repair, fluid balance, and energy metabolism. The shape and size of the nucleus helps in the light microscopic distinction of one glial cell type from another as their cytoplasmic process are often not apparent on H and E preparations and can be demonstrated only with the use of metallic impregnation.

Immunohistochemical or electron microscopic methods: astrocytes have round to oval nuclei with pale chromatin, found in white and gray matter. Star shaped appearance which is imparted by the multipolar, branching cytoplasmic processes that emanate from the cell body. The cytoplasm contain characteristic cytoplasmic intermediate filament protein called glial fibillary acidic protein (GFAP), this is seen by Immunohistochemical stain. Astrocytes are the major cell Type responsible for repair and scar formation in the brain.

- **Oligodendrocytes:** Have cytoplasmic process wrapped around the axons of neurons to form myelin. They have round small lymphocytes like nuclei.[(2)]
- **Ependymal cells:** Line the ventricular system.
- **Microglia:** Are mesoderm–derived cells that serve as fixed macrophages in CNS.

Neurons:

Nerve cells, or neurons, are independent anatomic and functional units with complex morphologic characteristics. They are responsible for the reception, transmission, and processing of stimuli; the triggering of certain cell activities; and the release of neurotransmitters and other signelling molecules.[2]

WHO Classification of Tumours of the CNS

- Neuroepithelial Tumors
  - Astrocytic tumors
  - Oligodemdroglial tumors
  - Ependymal tumors
  - Mixed gliomas
- Choroid plexus tumors
- Neurologic tumors
- Pineal parenchymal tumors
- Embryonal tumors
- Tumors of cranial/spinal nerves
- Mesenchymal tumors, benign
- Mesenchymal tumors, malignant
- Uncertain histogenesis
- Hemopoietic neoplasms
- Cysts/tumor like lesions
- Sellar tumors

TUMOURS OF THE MENINGES

- Tumours of meningothelial cells
- Meningioma

Gliomas

Astrocytomas:

Pilocytic astrocytoma:

Definition:

A relatively circumscribed, slowly growing, often cystic astrocytoma occurring in children and young adults,It is characterised histologicall by a biphasic pattern with varying proportions of compacted bipolar cells associated with Rosenthal fibers and loose-textured multipolar cells associated with micro cysts and eosinophilic granular bodies/hyaline droplets.[3]

ICD-O code: 9421/1

Grading: Pilocytic astrocytomas correspond to WHO grade1.[3]

Incidence:

Pilocytic astrocytomas comprise approximately 5-6% of all gliomas with an overall incidence of 0.37 per 100,000 persons per year. Pilocytic astrocytoma is the most common glioma in children, in whom the majority (67%) arise in cerebellum.[4]

Age and sex distribution:

Pilocytic astrocytoma most commonly develops, without a clear gender predilection, during the first two decades of life with an age-adjusted incidence rate 0.8 per 100 000 persons per year.[5]

Localization:

Pilocytic astrocytomas arise throughout the neuraxis; however, in the paediatric population more tumors arise in the infratentorial region.[10]Preferred sites include the optic nerve (optic nerve glioma),optic chiasm/hypothalamus, thalamus and basal ganglia, cerebral hemispheres, cerebellum (cerebellar astrocytoma) and brain stem (dorsal exophytic brain stem glioma). In the paediatric population, the most common supratentorial site is the hypothalamus/optic pathways followed by the thalamic/basal ganglia region. Large hypothalamic, thalamic, and brain stem lesions may largely occupy the ventricle, their site of origin being difficult to define.[10]

Clinical features:

Signs and symptoms:

Pilocytic astrocytomas produce focal neurological deficits or non-localizing signs, e.g. macrocephaly, headache, endocrinopathy, or increased intracranial pressure due to mass effect or ventricular obstruction.[3] Seizures are uncommon, since the lesions infrequently involve cerebral cortex. Given their slow rate of growth, the clinical presentation of pilocytic tumours is generally that of a slowly evolving lesion. Pilocytic astrocytomas of the optic pathways often produce visual loss.

Proptosis may be seen with intraorbital examples. Early radiologically detected lesions may be unassociated with visual symptoms or ophthalmologic deficits. Hypothalamic/ pituitary dysfunction, including obesity and diabetes insipidus is often but not invariably apparent large hypothalamic examples. Some hypothalamic-chiasmatic lesions of young children have been associated with leptomeningeal seeding and a poor outcome. It is unclear whether such tumours represent a distinct entity.(3)

Pilocytic astrocytomas of the thalamus present with signs of CSF obstruction or neurological deficits, such as hemiparesis, due to internal capsule compression. Cerebellar pilocytic astrocytomas usually present in the first two decades of life with clumsiness, worsening headache, nausea and vomiting. Brain stem examples usually cause hydrocephalus or signs of brain stem dysfunction. In contrast to diffuse astrocytoma of the pons, which produces symmetric “pontine hypertrophy” pilocytic tumours of the brain stem are usually dorsal and exophytic just into the cerebellopontine angle.(3)

Macroscopy:

Most pilocytic astrocytomas are soft, grey and rather discrete. lntra-or paratumoural cyst formation is common. Chronic lesions may contain calcium or haemosiderin deposits. Optic nerve tumours also often

show collar-like involvement of the subarachnoid space. Primary diffuse leptomeningeal pilocytic astrocytoma is a rarity.[7]

Histopathology:

This astrocytic tumour of low to moderate cellularity exhibits an often biphasic pattern with varying proportions of compacted bipolar cells with Rosenthal fibers and loose-textured multipolar cells with microcysts and granular bodies/hyaline droplets. Rare mitosis, hyperchromatic and pleomorphic nuclei, glomeruloid vascular proliferation, infarct-like necrosis and infiltration of leptomeninges are compatible with the diagnosis of pilocytic astrocytoma and are not signs of malignancy.[3]

Rosenthal fibers:

These tapered corkscrew-shaped, brightly eosinophilic, hyaline masses are intracytoplasmic in location, a fact best seen on smear. Rosenthal fibers are most common in compact, piloid tissue. They appear bright blue on a Luxol fast blue (LFB) stain. Although helpful in diagnosis, their presence is not required. Lastly, Rosenthal fibers are neither specific to pilocytic astrocytoma nor indicative of neoplasia.

They are often seen in gangliоglioma and are a common finding in chronic reactive gliosis. Densely fibrillar, paucicellular lesions containing Rosenthal fibers are as likely to be reactive gliosis as pilocytic astrocytoma. Ultrastructurally, Rosenthal fibers lie within astrocytic

processes and consist of amorphous, electron-dense elements surrounded by intermediate (glial) filaments. Being composed of α-β crystallin, they lack GFAP immunoreactivity at all but their fibral rich periphery.[3]

Vasculature:

Pilocytic astrocytomas are highly vascular, as is evidenced by their contrast enhancement.[3]

Regressive changes:

Given the indolent nature and often slow clinical evolution of pilocytic astrocytomas, it is not surprising that regressive changes are seen. Marked hyalinized, ectatic vessels are one such feature.[3]

Growth pattern:

As a rule, pilocytic astrocytomas are macroscopically somewhat discrete. Thus, when anatomy permits, e.g. cerebellum or cerebral hemispheres, many can be removed in toto.[3]

Infiltration of the meninges:

Involvement of the subarachnoid space is a common finding in pilocytic astrocytoma. It is not indicative of aggressive or malignant behaviour, nor does it portend subarachnoid dissemination.

In contrast, it is a characteristic, even diagnostically helpful feature. Leptomeningeal invasion occurs at any tumour site, but is particularly common in the cerebellum and optic nerve. In optic nerve, more so than in the cerebellum, the Ieptomeningeal component may be

reticulin-rich. Another typical pattern of extraparenchymal spread is extension into perivascular spaces.[3]

Distant spread and metastasis:

Surprisingly, otherwise typical pilocytic astrocytomas very occasionally seed the neuraxis, rarely even before the primary tumour is detected. The proliferation index in such cases varies but is usually low. Thus, this atypical behaviour of pilocytic astrocytoma cannot be predicted. The hypothalamus is the usual primary site. A related, less favourable lesion, the pilomyxoid astrocytoma, typically occurring in the hypothalamic region, more often undergoes craniospinal spread. This lesion is discussed below.[3]

Malignant transformation:

As a group, pilocytic astrocytomas are remarkable in maintaining their WHO grade I status over years and even decades. As a rule, alterations over time are in the direction of regressive change rather than of anaplasia. One large study found the acquisition of atypia, particularly of increased cellularity, nuclear abnormalities and occasional mitoses, to be of no prognostic significance.

There have, however, been rare examples of pilocytic astrocytoma undergoing malignant transformation.[3]

Prognostic and predictive factors:

As a group, pilocytic astrocytomas are slowly growing masses which may stabilize at any point in their evolution. Rare examples even spontaneously regress. Stability in tumour grade and differentiation is typically maintained for decades.[3]

Diffuse astrocytoma:

Definition:

A diffusely infiltrating astrocytoma that typically affects young adults and is characterized by a high degree of cellular differentiation and slow growth; the tumor occurs throughout the CNS but is preferentially located supratentorially and has an intrinsic tendency for malignant progression to anaplastic astrocytoma and ultimately, glioblastoma.[3]

ICD codes:[3]

- Diffuse astrocytoma 9400/3.
- Fibrillary astrocytoma 9420/3.
- Gemistocytic astrocytoma 9411/3.
- Protoplasmic astrocytoma 9410/3.

Grading:

Diffuse astrocytoma corresponds to WHO grade II. Although the gemistocytic variant appears to be particularly prone to progress to anaplastic astrocytoma and glioblastoma, the WHO Working Groups did

not recommend assigning it a WHO grade III as for anaplastic astrocytoma.[3]

Incidence:

Diffuse astrocytoma represents 10—15% of all astrocytic brain tumours, with an incidence rate of approximately 1.4 new cases/1 million population a year. Epidemiological data suggest that the incidence of astrocytoma in children has slightly increased during the past three decades in several Scandinavian countries and in North America.[12]

Age and sex distribution:

The age distribution of diffuse astrocytoma shows a peak incidence in young adults between ages 30 and 40. Approximately 10% occur below the age of 20, 60% between 20-45 years of age, and about 30% over 45 years of age with a mean of 34 years. There is a predominance of affected males (Male: Female ratio, 1.18: 1).[3]

Localization:

Diffuse astrocytoma may be located in any region of the CNS, but it most commonly develops supratentorially in the frontal and temporal cerebral lobes of both children and adults (one third of cases each). The brain stem and spinal cord are the next most frequently affected sites, while diffuse astrocytoma is distinctly uncommon in the cerebellum.[3]

Symptoms and signs:

Seizures are a common presenting symptom, although in retrospect subtile abnormalities such as speech difficulties, changes in sensation, vision, or some motor changes may have been present earlier. With frontal lobe tumours, changes in behaviour or personality may be the presenting feature. Any such change may have been present for months before diagnosis, but symptoms may also be abrupt in onset.[3]

Neuroimaging:

On CT scans, diffuse astrocytoma most often presents as ill-defined, homogeneous masses of low density without contrast enhancement. However, calcification, the cystic changes and even lower degrees of enhancement may be present early. MRI studies usually show hypodensity on T1-weighted and hyperintensity on T2-weighted images, with enhancement of the areas involved early in the evolution of the tumour. Gadolinium enhancement is uncommon in low-grade diffuse astrocytoma, but tends to appear during progression to anaplastic astrocytoma (WHO grade III).[3]

Macroscopy:

Because of their infiltrative nature, these tumours usually show blurring of the gross anatomical boundaries. There is enlargement and distortion, but not destruction, of the invaded anatomical structures, e.g. cortex and compact myelinated pathways. Local mass lesions may be

present in either grey or yellow-white matter, but they have indistinct boundaries, and changes such as smaller or larger cysts, granular areas and zones of firmness or softening may be seen. Cystic change most commonly appears as a focal spongy area, with multiple cysts of varying size. Extensive microcyst morphology formation may cause a gelatinous appearance. Occasionally, a single large cyst filled with clear fluid may be present. Tumours with prominent gemistocytes sometimes have single, large smooth-walled cysts. Focal calcification may also be present, and a more diffuse grittiness may be observed. Extension into contra-lateral structures, particularly in the frontal lobes, is also observed.[3]

Histopathology:

Diffuse astrocytoma is composed of well differentiated fibrillary or gemistocytic neoplastic astrocytes on the background of a loosely structured often microcystic tumour matrix. In comparison to normal brain, cellularity is moderately increased and occasional nuclear atypia is a typical feature. Mitotic activity is generally absent, and a single mitosis does not yet allow the diagnosis of anaplastic astrocytoma.[3] The presence of necrosis or microvascular proliferation is incompatible with the diagnosis of diffuse astrocytoma. Phenotypically, neoplastic astrocytes may vary considerably with respect to their size, the prominence and disposition of cell processes, and the abundance of

cytoplasmic glial filaments. The pattern may vary markedly in different regions of the neoplasm.

Histological recognition of neoplastic astrocytes using H&E staining on sectioned material depends mainly on nuclear characteristics. The normal astrocytic nucleus is oval to-elongate, but on sectioning, occasional round cross-sections are seen. It is typically vesicular with intermediate-sized masses of chromatin and often with a distinct nucleolus. Normal human astrocytes show no H&E stainable cytoplasm that is distinct from the background neuropil. Reactive astrocytes are defined by enlarged nuclei and the presence of stainable, defined cytoplasm, culminating in the gemistocyte, which has a mass of eosinophilic cytoplasm, often an eccentric nucleus, and a cytoplasm that extends in to fine processes.

Differential diagnosis: The diffuse astrocytoma contains astrocytes that are increased in number and also usually in size, but are otherwise difficult to distinguish on an individual basis from the normal or reactive cells. In minor degrees of anaplasia, it is their number and, most commonly, the monotony of their morphology that is the most helpful in recognizing their neoplastic nature.

Fibrillary astrocytoma:

This most frequent histological variant of astrocytoma is predominantly composed of fibrillary neoplastic astrocytes. Nuclear

atypia is diagnostic criterion but mitotic activity, necrosis and microvascular proliferation are absent. A single mitosis does not allow the diagnosis of anaplastic astrocytomà. The occasional or regional occurrence of gemistocytic neoplastic cells is compatible with the diagnosis of fibrillary astrocytoma cell density is low to moderate. The cytoplasm is often scant and barely discernible, creating the appearance of naked nuclei. Nuclear atypia (i.e. enlarged, cigar-shaped, or irregular hyperchromatic nuclei) is a histological hallmark distinguishing tumour cells from normal and reactive astrocytes. Even prominent nuclear atypia is compatible with the diagnosis of diffuse astrocytoma WHO grade II so long as mitoses are very rare or absent.[13]

Immunohistochemistry: Glial fibrillary acidic protein (GFAP) is consistently expressed.[3]

Gemistocytic astrocytoma:

This variant is astrocytoma is characterized by presence of a conspicuous, though variable, fraction of gemistocytic neoplastic astrocytes. Gemistocytes should amount to more than approximately 20% of all tumour cells.[14]

Immunohistochemistry: the gemistocytic neoplastic astrocytes consistently express GFAP in their perikarya and cell processes.[3]

Protoplasmic astrocytoma:

This rare variant is predominantly composed of neoplastic astrocytes showing a small cell body with a few flaccid processes with a low content of glial filaments and scant GFAP expression. Cellularity is low and mitotic activity absent. Mucoid degeneration and microcyst formation are common and characteristic features.[3]

Immunohistochemistry: GFAP imunostaining is variable and generally low.

Anaplastic astrocytoma:

Definition:

A diffusely infiltrating, malignant astrocytoma that primarily affects adults, preferentially located in the cerebral hemispheres, and that is histologically characterized by nuclear atypia, increased cellularity and significant proliferative activity. The tumour may arise from diffuse astrocytoma WHO grade II or de novo, i.e., without evidence of a less malignant precursor lesion, and has an inherent tendency to undergo progression to glioblastoma.[3]

ICD-O code: 9401/3.

Grading: Anaplastic astrocytoma corresponds to WHO grade Ill.[3]

Localization:

The localization of anaplastic astrocytoma corresponds to that of other diffuse infiltrating astrocytomas, with a preference to the cerebral hemisphere.[3]

Histopathology:

The principle histopathological features are those of a diffusely infiltrating astrocytoma with increased cellularity as compared to the grade II equivalent, distinct nuclear atypia and mitotic activity.

Glioblastoma:

Definition:

The most frequent primary brain tumour and most malignant neoplasm with predominant astrocytic differentiation; histopathological feature include nuclear atypia, cellular pleomorphism, mitotic activity, vascular thrombosis, microvascular proliferation and necrosis.[3]

ICD-O code: 9440/3.

Grading: WHO grade IV.

Age and sex distribution:

Glioblastoma may manifest at any age, but preferentially affects adults, with a peak incidence at between 45 and 75 years of age.[15]

Localization: Glioblastoma occurs most often in the subcortical white matter of cerebral hemisphere.[3]

Clinical features:

The clinical history of the disease is usually short (less than 3 months in more than 50% of cases.[3]

Multifocal glioblastomas:

Although multifocally is not unusual when defined radiologically, the incidence of truly multiple, independent gliomas occurring outside the setting of inherited neoplastic syndromes is unclear.[16]

Primary and secondary glioblastoma:

The terms primary and secondary glioblastoma were first used by Scherer in 1940 who noted “from a biological and clinical point of view, the secondary glioblastomas developing in astrocytomas must be distinguished from “primary” glioblastomas; they are probably responsible for most of the glioblastomas of long clinical duration”. The majority of glioblastomas (>90%) develop very rapidly with a short clinical history (usually <3 months), without clinical or histological evidence of a pre-existing, less malignant precursor lesion (primary or de novo glioblastoma). They typically develop in older patients (mean, 62 years).[4,17]

Histopathology:

Glioblastoma is anaplastic, cellular glioma composed of poorly differentiated, often pleomorphic astrocytic tumour cells with marked nuclear atypia and brisk mitotic activity. Prominent microvascular

proliferation and/or necrosis are essential diagnostic features. As the term glioblastoma “multiforme” suggests, the histopathology of the tumour is extremely variable.[18]

Tissue patterns:

The diagnosis of glioblastoma is typically based on the tissue pattern rather than on the identification of certain cell types. The presence of highly anaplastic glial cells, mitotic activity and vascular proliferation and/or necrosis is required.[3]

Epithelial structure:

Occasionally, glioblastoma contains foci with glandular and ribbon-like epithelial structures. These elements have a large oval nucleus, prominent nucleus, prominent nucleolus and round, well-defined cytoplasms. They are also referred to as “adenoid” glioblastoma.[19]

Small cell glioblastoma: although small cells are common in glioblastoma, they are predominant or exclusive in a subset known as “small cell glioblastoma.[3]

Glioblastoma with oligodendroglioma component: Occasional glioblastomas contain foci that resemble oligodendroglioma.

Multinucleated giant cells: Large, multinucleated tumour cells are often considered a hallmark of glioblastomas and occur with a spectrum of increasing size and pleomorphism.[21]

- **Gemistocytes:** At the other extreme of glioblastoma differentiation are "gemistocytes" and the related "fibrillary astrocyte", recognizing that transition forms connect these two types.[3]
- **Granular cells:** Large cells with a granular, periodic acid-Schiff (PAS) positive cytoplasm may occur scattered within glioblastoma.
- **Lipidized cells:** Cells with a foamy cytoplasm are another feature occasionally observed in glioblastoma.[19]
- **Perivascular lymphocytes:** Perivascular lymphocyte cuffing occurs in a minority of glioblastomas. The inflammatory cells have been phenotypically characterized on the basis of their immunoreactivity.
- **Metaplasia:** Adenoid and squamous epithelial metaplasia are more common in gliosarcoma than in the ordinary glioblastoma.[23]
- **Microvascular proliferation:** In addition to necrosis, the presence of microvascular proliferation (previously called endothelial cell proliferation) is a histopathological hallmark of glioblastoma. On light microscopy classic microvascular proliferations typically appear as "glomeruloid tufts".[3]`
- **Proliferation:** Proliferative activity is usually prominent. Atypical mitoses are frequently present.[3]
- **Angiogenesis:** Glioblastomas are among the most vascularized tumours in humans.[24]

- **Necrosis:** Tumour necrosis is a fundamental feature of glioblastoma. Necrosis can be seen by neuroimaging as a non-enhancing core.[3]

Giant cell glioblastoma:

Definition:

A histological variant of glioblastoma with a predominance of bizarre, multinucleated giant cells, an occasionally abundant stromal reticulin network and a high frequency of TP53 mutations.[3]

ICD-O code: 9441/3.[3]

Grading: Giant cell glioblastoma corresponds histologically to WHO grade IV.[3]

Incidence:

Giant cell glioblastoma is a rare variant that accounts for less than 1% of all brain tumours and up to 5% of glioblastoma.[25]

Age and sex distribution:

In a series of 55 cases, the mean age at clinical manifestation was 41 years. Males and females are equally affected (M/F ratio 1: 1).

Clinical features:

Symptoms and signs:

Symptoms are similar to those of the ordinary glioblastoma.[3]

Neuroimaging:

Giant cell glioblastomas are distinctive because of their circumscription and firmness caused by the marked production of tumour

stroma. They are often located subcortically in the temporal and parietal lobes. On CT and MTI, they may mimic a mtastasis.[3]

Oligodendroglial tumours:

Oligodendroglioma:

Definition: A diffusely infiltrating, well-differentiated glioma of adults, typically located in the cerebral hemispheres, composed of neoplastic cells morphologically resembling oligodendroglia and often harbouring deletions of chromosomal arms 1p and 19q.[3]

ICD-O code: 9450/3.[3]

Grading:

Oligodendroglioma corresponds histologically to WHO grade II.[3]

Incidence:

Oligodendroglioma accounts for approximately 2.5% of all primary brain tumours and 5-6% of all gliomas.[4,5]

Age and sex distribution:

The majority of oligodendroglioma arise in adults, with a peak incidence between 40 and 45 years of age. Oligodendroglioma is rare in children accounting for only 2% of all brain tumours in patients younger than 14 years. Males affected slightly more than females, with ratio of (1.1 : 1).[5]

Localization:

Oligodendroglioma arise preferentially in the cortex and white matter of the cerebral hemispheres. The frontal lobe is involved in 50-65% of the patients followed with decreasing frequencies the temporal, parietal and occipital lobes. Patients have been reported with oligodendroglioma in the posterior fossa, basal ganglia, brain stem or spinal cord as well as primary leptomeningeal oligodendroglioma and oligodendroglia gliomatosis cerebri.[34]

Clinical features:

Symptoms and signs:

Approximately two third of the patients present with seizures. Further common presentations include headache and other signs of increased intracranial pressure..[3]

Neuroimaging:

On CT oligodendroglioma usually appears as hypo-or isodense, well demarcated mass lesions.[3]

Macroscopy:

Oligodendroglioma usually appears as well defined soft masses of grayish-pink colour.

Histopathology:

Oligodendroglioma are diffusely infiltrating gliomas of moderate cellularity that are composed of monomorphic cells with uniform round

nuclei and perinuclear halos on paraffin sections (honeycomb appearance). Additional features include microcalcifications, mucoid/cystic degenerationand adense network of branching capillaries.[3]

Immunohistochemistry:

There is no immunohistochemical marker available that allows the specific and sensitive recognition of human oligodendroglioma tumour cells.[35]

Genetic susceptibility:

Occasionally familial clustering of oligodendroglioma has been reported, example, include two brothers, mother and daughter, twin sisters and a father and son.[3]

Genetic:

The vast majority showed normal or non-clonal karyotypes.[36]

Anaplastic oligodendroglioma:

Definition:

An oligodendroglioma with focal or diffuse histological features of malignancy and a less favourable features of malignancy and a less favourable prognosis.[3]

ICD-O code: 9451/3.[3]

Grading:

Anaplastic oligodendroglioma corresponds histologically to WHO grade III. Anaplastic features that have been linked to malignancy in

oligodendroglioma are high cellularity, marked cytological atypia, high mitotic activity, microvascular proliferation and necrosis with or without pseudopalisading.

Incidence:

Anaplastic oligodendroglioma accounted for approximately 1.2% of primary brain tumours and adjusted annual incidence rates ranging from 0.07 to 0.18 per 100,000 population have been reported.[5,4]

Age and sex distribution:

Anaplastic oligodendroglioma manifests preferentially in adults, with a peak incidence between 45 and 50 years of age.[5,4] Anaplastic oligodendroglioma shows a slight male predominance, with a male : female ratio of 1.1 : 1 reported in a population-based series of 781 patients.[3]

Localization:

Anaplastic oligodendroglioma shares with WHO grade II oligodendroglioma a preference for the frontal lobe, followed by the temporal lobe.[3]

Clinical features:

Anaplastic oligodendroglioma may develop either due to novo or by progression from a pre-existing WHO grade II oligodendroglioma. The preoperative history of patients with de novo tumours is usually short with seizures being the most common presenting symptom.[3]

Neuroimaging

Anaplastic oligodendroglioma may show heterogeneous patterns,owing to the variable presence of necrosis, cystic degeneration, intratumoural hemorrhages and calcification. Contrast enhancement on CTand MRI is usual and may be patchy or homogeneous. Ring-enhancement is uncommon and when present, heralds a poor prognosis.[37]

Macroscopy:

The macroscopic features are similar to those of WHO grade II oligodendroglioma expect that anaplastic oligodendroglioma may demonstrate areas of tumour necrosis.[3]

Histopathology:

Anaplastic oligodendroglioma is a cellular, diffusely infiltrating glioma that may show considerable morphological variation. The majority of tumour cells demonstrate features that are reminiscent of oligodendroglial cells, i.e. rounded hyperchromatic nuclei, perinuclear halos, and few cellular processes. Focal microcalcifications are often present. Mitotic activity is usually prominent. Occasional tumours are characterized by marked cellular pleomorphism with multinucleated giant cells or have a conspicuous spindle-cell appearance.[3]

Genetics:

Chromosomal and array-based comparative genomic hybridization studies have revealed total losses of 1 p and 19q in up to two thirds of anaplastic oligodendrogliomas, which is slightly less common than in WHO grade II oligodendroglioma.[3)]

Ependymal tumours:

Subependymoma:

- **Definition:** A slowly growing, benign neoplasm, typically attached to a ventricular wall, compared of glial tumour cell clusters embedded in an abundant fibrillary matrix with frequent microcystic change.[(3)]
- **ICD-O code:** 9383/1.[(3)]
- **Grading:** Subependymoma corresponds histologically to WHO gradeI.[(3)]
- **Incidence:** The true incidence of subependymoma is difficult to determine, because these tumours frequently remain asymptomatic and are often found incidentally at autopsy. In two studies, they accounted for approximately 8% of ependymal tumours.[(41)]
- **Age and sex distribution:** Subependymoma develop in both sexes and in all age groups, but occur most frequently in middle-aged and elderly patients.[(3)]

- **Localization:** The most frequent site is the fourth ventricle, followed by the lateral ventricles.[3]
- **Clinical features:**
  - ***Symptoms and signs:*** Subependymoma may become clinically apparent through ventricular obstruction and raised intracranial pressure.[3]
  - ***Neuroimaging:*** subependymoma are sharply demarcated, nodular masses that are usually non-enhancing. Calcification and foci of haemorrhage may be apparent.[42]
  - ***Macroscopy:*** These tumours present as firm nodules of variable size, bulging into the ventricular lumen in most instances, the diameter does not exceed 1-2 cm.[3]

Myxopapillary ependymoma:

- **Definition:** A slowly growing, ependymal glioma with preferential manifestation in young adults and almost exclusive location in the region of conus medullaris, cauda equina and filum terminale of the spinal cord, typically characterized histologically by tumour cells arranged in a papillary manner around vascularized myxoid stromal cores.[3]

- **ICD-O code:** 9394/1.[3]
- **Grading:** These slowly growing tumours have a favourable prognosis and corresponds to WHO grade I. Anaplastic variants are virtually unknown.[3]
- **Incidence:** Among all ependymomas, the frequency of myxopapillary variants is 9-13%.[41]
- **Age and sex distribution:** An average age at manifestation of 36 years has been reported with abroad range between 6 and 82 years. Male to female ratio was 2.2 : 1.[3]
- **Localization:** Myxopapillary ependymomas occurs almost exclusively in the conus medullaris-cauda equine-filum terminale region. It can be observed at other locations such as the cervical-thoracic, spinal cord, the fourth ventricle, the lateral ventricle or the brain parenchyma.[3]
- **Histopathology:** Myxopapillary ependymomas are characterized by GFAP-expressing, cuboidal to elongated tumour cells radially arranged in a papillary manner around vascularized stromal cores. Some tumours, however, show minimal or no papillary areas and instead feature fascicles of more elongated cells.[3]
- **Immunohistochemistry:** for GFAP, S-100 and vimentin are positive.[3]

Ependymoma:

- **Definition:** A generally slowly growing tumour of children and young adults, originating from the wall of the ventricles of from the spinal canal and composed of neoplastic ependymal cells.[3]
- **ICD-O code:**[3]

  - Ependymoma 9391/3
  - Cellular ependymoma 9391/3
  - papillary ependymoma 9393/3
  - Clear cell ependymoma 9391/3
  - Tanycytic ependymoma 9391/3

- **Grading:**

  Ependymoma corresponds histologically to WHO grade II.[3]

- **Incidence:** In the United States, WHO grade II –III ependymomas have an approximate incidence of 0.29 in males and 0.22 per 1000, 000 persons per year in females.[5]
- **Age and sex distribution:** Ependymomas develop in all age groups with a range from 1 month to 81 years, but incidence is greately affected by histological type and location. Intratentorial ependymomas predominate in children, with a mean age at clinical manifestation of 6.4 years and a range of 2 month to 16 years. A second age peak at 30 – 40 years has been reported for spinal tumours. Supratentorial ependymomas affect paediatric as well as adult patients.

- **Etiology:** The identification of SV40 virus large T antigen-related DNA sequences in a significant proportion of human choroid plexus papillomas and ependymomas received attention since it was thought possible to reflect latent infection, following widespread use of SV40-contaminated polio vaccines during 1955 -1962.
- **Localization:** These tumours may occur at any site along the ventricular system and in the spinal canal. They most commonly develop in the 4^{th} ventricles and in the spinal cord, following by the lateral ventricles and the third ventricle in adults. Rare extraneural ependymomas have been observed in the ovaries.(41)
- **Macroscopy:** Ependymoma are typically soft tan masses with well-demarcated borders visible foci of haemorrhage or necrosis are uncommon.(3)
- **Histopathology:** The most common or classic, pattern of ependymoma is a well-delineated, moderately cellular glioma with a monomorphic, nuclear morphology, characterized by round to oval nuclei with “salt and pepper” speckling of the chromatin. Mitoses are rare or absent. Apart from the nuclear aspects, key histological features are perivascular pseudorosettes and ependymal rosettes. perivascular pseudorosettes originate from tumour cells arranged radially around blood vessels with perivascular anuclear zones of gilal fibrillary protein (GFAP)-rich fibrillary processes.(3)

- **Cellular ependymoma:** this variant is more common extraventricular locations and shows conspicuous cellularity without a significant increases in mitotic rate.[3]
- **Papillary ependymoma:** Ependymomas form linear, epithelial-like surfaces along their CSF exposures.[3]
- **Clear cell ependymoma:** Clear cell ependymomas display an oligodendroglia-like appearance with clear perinuclear halos. This variant appears to be preferentially located in the supratentorial compartment of young patients.[3]
- **Tanycytic ependymoma:** Tanycytic tumours are most commonly, found in the spinal cord.It is para ventricular,with elongated cytoplasmic processes that extend to ependymal surface.
- **Other pattern:** Rare ependymoma variants include ependymoma with lipomatous differentiation, giant cell ependymoma, ependymoma with extensive tumour cell vacuotation, melanotic ependymoma, signet ring cell ependymoma, ovarian ependymoma, ependymoma with neuropil-like islands and ganglioglioma with a tanycytic glial component.[3]

Immunohistochemistry: The great majority of ependymomas display GFAP immunoreactivity with a prominent reaction for GFAP usually observed in pseudorosettes.

Anaplastic ependymoma:

- **Definition:** malignant glioma of ependymal differentiation with accelerated growth and unfavourable clinical outcome, particularly in children, histologically characterized by high mitotic activity, often accompanied by microvascular proliferation and pseudopalisading necrosis.[3]
- **ICD-O code:** 9392/3.[3]
- **Grading:** Anaplastic ependymoma corresponds histologically to WHO grade III.[3]
- **Incidence:** Incidence data vary considerably due to the uncertainly regarding histological criteria of malignancy. Anaplastic changes are far more frequent in childhood intracranial ependymomas, particularly posterior fossa examples, than in those of the spinal cord.[5]
- **Clinical features:** Signs and symptoms of anaplastic ependymomas are similar to those of ependymoma WHO grade II.
- **Histopathology:** Anaplastic ependymoma show increased cellularity and brisk mitotic activity, often associated with microvascular proliferation and pseudopalisading necrosis**.**

Embryonal tumours:

1- Medulloblastoma:

- ***Definition:*** A malignant, invasive embryonal tumour of the cerebellum with preferential manifestation in children, predominantly neuronal differentiation, and an inherent tendency to metastasize via CSF pathways.[3]
- ***ICD-O code:***[3]

- Medulloblastoma	9470/3.
- Desmoplastic/nodular medulloblastoma	9471/3.
- Medulloblastoma with extensive nodularity	9471/3.
- Anaplastic medulloblastoma	9474/3.
- Large cell medulloblastoma	9474/3.

- ***Grading:*** Medulloblastomas correspond histologically to WHO grades IV.[3]
- ***Age and sex distribution:*** The peak age at presentation is 7 years. Approximately 65% of patients are males.[3]
- ***Etiology:*** Different polyomaviruses have been discussed as possible causative agents.[3]
- ***Localization:*** At least 75% of childhood medulloblastomas arise in the vermis, and project into the fourth ventricle. Involvement of cerebellar hemispheres increases with the age of the patient.[3]

- ***Histolopathology:*** Medulloblastoma is composed of densely packed cells with round-to-oval or carrot shaped hyperchromatic nuclei surrounded by scanty cytoplasm. Neuroblastic (Homer Wright) rosettes, which are observed in less than 40% of cases, are often associated with marked nuclear pleomorphism and high mitotic activity.[(3)]
- ***Desmoplastic/nodular medulloblastoma:*** This variant is characterized by nodular, reticulin-free zones (pale islands) surrounded by densely packed, highly proliferative cells with hyperchromatic and moderately pleomorphic nuclei which produce a dense intercellular reticulin fiber network.[(50)]
- ***Medulloblastoma with extensive nodularity:*** The medulloblastoma with extensive nodularity, which was previously designated “cerebellar neuroblstoma” occurs in infants and differs from the related desmoplastic/nodular variant by having an expanded lobular architecture.[(51)]
- ***Anaplastic medulloblastoma:*** Marked nuclear pleomorphism, nuclear moulding, cell-cell wrapping and high mitotic activity, often with atypical forms, are characteristics of this variant.[(52)]
- ***Large cell medulloblastoma:*** The large cell variant represents approximately 2-4% of medulloblastomas. The term derives from its monomorphic cells with large, round vesicular nuclei, prominent nucleoli and variable amount of eosinophilic cytoplasm.[(3)]

Myogenic differentiation:

- ***Synonym:*** medullomyoblastoma (ICD-O: 9472/3): Medulloblastoma with myogenic differentiation was previously termed medullomyoblastoma. However, genetic changes in medulloblastoma with myogenic differentiation are similar to those in other medulloblastomas, this is not adistinct entity.[3]

Melanotic differentiation:

- ***Synonym:*** Melanocytic medulloblastoma (ICD-O: 9470/3): Medulloblastoma with melanotic differentiation was previously termed melanocytic medulloblastoma. However, groups of melanotic tumour cells can occur in different variants of medullobatoma and the therefore, this is not regarded as a separate variant.[3]
- ***Immunohistochemistry:*** The frequent differentiation of the medulloblastoma along neuronal lineage manifests immunophenotypically as expression of neuronal antigens. Class III β-tubulin, microtubule-associated protein 2, neuron specific enolase (NSE) and synaptophysin.[3]

Central nervous system primitive neuroectodermal tumours:

- ***Definition:*** A heterogeneous group of tumours occurring predominantly in children and adolescents. They may arise in the cerebral hemispheres, brain stem, spinal cord and are composed of undifferentiated or poorly

differentiated neuroepithelial cells which may display divergent differentiation along neuronal, astrocytic and ependymal lines. CNS/supratentorial PNET is an embryonal tumour composed of undifferentiated or poorly differentiated neuroepithelial cells. Tumours with only neuronal differentiation are termed cerebral neuroblastomas or, if ganglion cells are also present, cerebral ganglioneuroblastomas. Tumours that recreate features of neural tube formation are termed medulloepitheliomas. Tumours with ependymoblastic rosettes are termed ependymoblastomas. Features common to all CNS PNET variants include early onset and aggressive clinical behavious.[3]

- **ICD-O codes:** [3]

  - CNS PNET, NOS 9473/3.
  - CNS Neuroblastoma 9500/3.
  - CNS ganglioneuroblastoma 9490/3.
  - Medulloepithelioma 9501/3.
  - Ependymoblastoma 9392/3.

- ***Grading:*** As with other embryonal brain tumours all CNS PNETs correspond histologically to WHO grades IV.[3]

Medulloepithelioma:

- ***Definition:*** a rare, malignant embryonal brain tumour affecting young children, histologically characterized by papillary, tubular or trabecular

arrangements of neoplastic neuroepithelium mimicking the embryonic neural tube.[3]

- ***Age and sex distribution:*** Medulloepitheliomas are rare tumours that typically affect children between 6 months and 5 years, with half occurring during the first two years.[53]
- ***Localization:*** Medulloepitheliomas develop in both the supra-and infratentorial compartments.[53]
- ***Histopathology:*** Medulloepitheliomas are malignant neoplasma that mimic the embryonic neural tube and are characterized by papillary, tubular or trabecular arrangements of neoplastic neuroepithelium with an external limiting membrane. These tumours often display multiple lines of differentiation, including neural glial and mesenchymal elements.[54]

Ependymoblastoma:

- ***Definition:*** a rare, malignant embryonal brain tumour manifesting in neonates and young children, histologically characterized by distinctive multilayered rosettes.[3]
- ***Age and sex distribution:*** consistent with the primitive neuroepithelial nature of the tumour, the ependymoblastoma occurs in young children, including neonates.[55]

Atypical teratoid/rhabdoid tumour:

- ***Definition:*** A highly malignant CNS tumour predominantly manifesting in young children, typically containing rhabdoid cells, often with primitive neuroectodermal cells and with divergent differentiation along epithelial, mesenchymal, neuronal or glial lines, associated with inactivation of the IN1/hSNF5 gene in virtually all cases.[3]
- ***ICD-O code:*** 9508/3.[3]
- ***Grading:*** This tumour corresponds to WHO grade IV.[3]

Tumours of the cranial and paraspinal nerves:

- ***Definition:*** A benign nerve sheath tumour that is typically encapsulated and composed entirely of well-differentiated Schwann cells. Multiple schwannomas are associated with neurofibromatosis type 2 or schwannomatosis.[3]
- ***CD-O code:*** 9560/0.
- ***Grading:*** Conventional, non-melanotic schwannoma corresponds histologically to WHO grade I.[3]
- **Synonyms:** Neurilemoma and neurinoma.[3]
- ***Incidence:*** Schwannomas represent 8% of intracranial tumours.[56]
- ***Age and sex distribution:*** All ages are affected but paediatric cases are rare. The peak incidence is in the fourth to sixth decade of life. Most

studies show no gender predilection, but some series have shown a female.[56]

- ***Localization:*** Intracranial schwannomas show a strong predilection for the eighth cranial nerve in the cerebellopontine angle.[3]

Neurofibroma:

- ***Definition:*** A well-demarcated intraneural or diffusely infiltrative extraneural tumour consisting of a mixture of cell types, including Schwann cells, perineurial-like cells, and fibroblasts; multiple and plexiform neurofibromas are typically associated with neurofibromatosis type 1.[3]
- ***ICD-O codes:*** [3]
  - Neuiofibroma 9540/0.
  - Plexiform neurofibroma 9550/0.
- ***Grading:*** Neurofibroma corresponds histologically to WHO grade I.[3]
- ***Incidence:*** Neurofibromas are common and occur either as sporadic solitary nodules unrelated to any apparent syndrome or, far less frequently, as solitary, multiple or numerous lesions in individuals with neurofibromatosis type 1 (NFl).
- ***Age and sex distribution:*** All ages and both sexes are affected.[3]

Meningiomas:

- ***Definition:*** MeningotheliaI (arachnoidal) cell neoplasm, typically attached to the inner surface of the dura mater.[3]
- ***ICD-O code:*** Meningioma 9530/0.[3]
- ***Grading:*** Most meningiomas are benign and correspond to WHO grade I. Certain histological subtypes or meningiomas with specific compinations of morphologic parameters are associated with less favoureble clinical outcomes and correspond to WHO grades II (atypical) and Ill (anaplastic or malignant).[3]
- ***Incidence:*** Meningiomas account for about 24—30% of primary intracranial tumours occurring in the USA. Meningiomas are often multiple in patients with neurofibromatosis type 2 (NF2).[5]

Meningiomas grouped by likelihood of recurrence and grade

Meningiomas with low risk of recurrence and aggressive growth		
Meningothelial meningioma	WHO grade I	9531/0
Fibrous (fibroblastic) meningioma	WHO grade I	9532/0
Transitional (mixed) meningioma	WHO grade I	9537/0
Psammomatous meningioma	WHO grade I	9533/0
Angiomatous meningioma	WHO grade I	9534/0
Microcystic meningioma	WHO grade I	9530/0
Secretory meningioma	WHO grade I	9530/0
Lymphoplasmacyte-rich meningioma	WHO grade I	9530/0
Metaplastic meningioma	WHO grade I	9530/0
Meningiomas with greater likelihood of recurrence and/or aggressive behavior		
Chordoid meningioma	WHO grade II	9538/1
Clear cell meningioma (intracranial)	WHO grade II	9538/1
Atypical meningioma	WHO grade II	9539/1
Papillary meningioma	WHO grade III	9538/3
Rhabdoid meningioma	WHO grade III	9538/3
Anaplastic (malignant) merningioma	WHO grade III	9530/3

- ***Age and sex distribution:*** Meningiomas occur most commonly in middle-aged and elderly patients, with peak during the sixth and seventh decades. Nonetheless, they also occur in children and the elderly.

Childhood examples tend to include more aggressive forms of meningioma.[3]

- ***Etiology:*** Meningiomas are known to be induced by low-moderate and high-dose radiation with an average time interval to tumour appearance of 35, 26 and 19—24 year. The majority with radiation-induced meningiomas have a history of low-dose irradiation (800 rad) to the scalp for tinea capitis.[3]
- ***Localization:*** The vast majority of meningiomas arise in intracranial, intraspinal or orbital locations. Intraventricular and epidural examples are uncommon. Within the cranial cavity, most meningiomas occur over the cerebral convexities, often parasagittal in association with the falx and venous sinus. Other common sites include the olfactory grooves, sphenoid ridges, para/suprasellar regions, optic nerve sheath, petrous ridges, tentorium and posterior fossa. Among other sites, metastases of malignant meningiomas most often involve lung, pleura, bone and liver.[3]
- ***Clinical features:***

  - ***Symptoms and signs:*** Meningiomas are generally slowly growing and produce neurological signs and symptoms by compression of adjacent structures. Headache and seizures often herald the presence of a meningioma.[3]

- ***Neuroimaging***: On MRI, meningiomas are typically isodense, contrast-enhancing dural masses. Calcification is best seen on CT scan. A characteristic feature of meningiomas is the so-called ‘dural tail’ surrounding the dural perimeter of the mass.[3]
- ***Histopathology:*** Meningothelial, fibrous and transitional meningiomas are the most common.[3]
  - ***Fibrous (fibroblastic) menmgioma:*** Uncommon in pure form, this meningioma variant consists of spindle cells forming parallel, storiform and interlacing bundles in a collagen-rich matrix.[3]
  - ***Transitional (mixed) meningioma:*** These common tumours feature the coexistence of meninothelial and fibrous patterns as well as transitions between these pattern.[3]
  - ***Psammomatous meningioma:*** This designation is applied to meningiomas containing a predominance of psammoma bodies over that of the tumour cells which give rise to them.[3]
  - ***Angiomatous meningioma:*** This meningioma variant feature, predominance of blood vessels over that of the tumour cells.[57]
  - ***Microcystic meningioma:*** This variant is characterized by cell with thin, elongate processes encompassing microcysts containing pale, eosinophilic mucinous fluid.

- ***Secretory meningioma:*** The hallmark of this tumour variant is the presence of focal epithelial differentiation in the form of intracellular lumina containing PAS-positive, eosinophilic secretion.[58]
- ***Metaplastic meningioma:*** A meningioma with striking focal or widespread mesenchymal components including osseous, cartilaginous, lipomatous, myxoid or xanthomatous tissue, singly or in combinations.[3]
- ***Chordoid meningioma:*** A meningioma variant consisting predominantly of tissue histologically similar to chordoma, featuring cords or trabeculae of eosinophilic, often vacuolated cells in an abundant mucoid matrix background.[59]
- ***Clear cell meningioma:*** An often patternless meningioma composed of polygonal cells with clear, glycogen-rich cytoplasm and prominent blocky perivascular and interstitial collagen.[3]
- ***Atypical meningioma:*** A meningioma with increased mitotic activity or three or more of the following histologic features: increased cellularity, small cells with a high nuclear cytoplasmic ratio, prominent nucleoli, uninterrupted patternless or sheet-like growth, and foci of spontaneous or geographic necrosis. Increase mitotic activity, is defined as 4 or more mitoss per 10 high-power (40x) field (defined as 0.16 mm^2).[60]

- ***Papillary meningioma*:** A rare meningioma variant defined the presence of a perivascular pseudopapillary pattern comprising the majority of the tumour.
- **Rhabdoid meningioma:** An uncommon tumour predominantly containing sheets of rhabdoid cells, i.e., plump cells with eccentric nuclei, often open chromatin, prominent nucleolus, and prominent inclusion-like eosinophilic cytoplasm appearing either as discernible whorled fibrils compact and waxy.[61]
- ***Anaplastic (malignant) meningioma:*** A meningioma exhibiting histological features of frank malignancy far in excess of the abnormalities present in atypical meningioma.[3]
- ***Immunohistochemistry*:** The vast majority of meningiomas stain for epithelial membrane antigen. (EMA). Vimentin positivity is found in all meningiomas.

Mesenchymal, non-meningothelial tumours:

- ***Definition:*** Benign and malignant mesenchymal tumours originating in the CNS and histologically corresponding to tumours of soft tissue or bone.[3]
- ***Grading:*** According to their histolkogical features and clinical behaviour, they range from benign neoplasms (WHO grade I) to highly malignant sarcomas (WHO grade IV).[3]

Tumours of adipose tissue:

- **Lipoma:** This benign lesion microscopically resembles normal adipose tissue.[3]
- **Angiolipoma:** The proportion of adipose cells and vasculature varies in this lipoma variant.[3]
- ***Hibernoma:*** This lipoma variant is rare in the CNS. It resembles brown fat and composed of uniform granular or multivacuolated cells with small, centrally placed nuclei.[3]

Fibrous tumours:

- ***Fibromatosis:*** This locally infiltrative but cytologicaly benign.[62]
- ***Solitary fibrous tumour:*** This lesion affects both cranial and spinal meninges. Its spindle cells are disposed in fascicles between prominent, eosinophilic bands of collagen.[3]
- ***Fibrosarcoma:*** This rare, malignant tumour shows interlacing bundles of spindle cells disposed in “herringbone” pattern.[3]

Fibrohistiocytic tumours:

- ***Benign fibrous histocytoma:*** This lesion is composed of a mixture of spindled (fibroblast-like) and plump (histiocyte-like) cells arranged in a storiform pattern.[3]

- ***Malignant fibrous histiocytoma (MFH):*** This neoplasm consists of spindled, plump and pleomorphic giant cells that can be arranged in a storilorm or fascicular pattern.[3]

Myogenic tumours:

- ***Leiomyoma:*** Most benign smooth muscle tumours are readily recognized by their pattern of intersecting fascicles composed of eosinophilic spindle cells with blunt-ended nuclei.[3]
- ***Lelomyosarcoma:*** Intracranial leiomyosarcomas correspond histologically to their soft-tissue counterparts.[3]
- ***Rhabdomyoma:*** This lesion consists entirely of mature striated muscle.[3]
- ***Rhabdomyosarcoma:*** Whether meningeal or parenchymal, nearly all CNS rhabdomyosarcomas are of the embryonal type.[3]
- ***Osteocartilaginous tumours:*** These benign osteocartilaginous tumours are usually dural-based; outside the CNS, they often develop in the skull and only secondarily displace dura and brain. Histologically, they correspond to similar tumours arising in bone, but are to be separated from asymptomatic dural calcification, ossification related to metabolic disease or trauma.[3]
- ***Mesenchymal chondrosarcoma:*** This neoplasm more often arises in bones of the skull or spine than within dura or brain parenchyma.[3]

- ***Osteosarcoma:*** Preferred sites are the skull or spine and, more rarely, the meninges or the brain.[3]
- ***Vascular tumours:*** Most vascular lesions of the central nervous system are malformative in nature and include arteriovenous malformation, cavernous angioma, venous angioma and capillary teleangiectasis.[3]
- ***Haemangioma:*** These lesions vary in size from microscopic to massive.[3]
- ***Epithelioid haemangioendothelioma*:** Skull base, dura or brain are rare locations for this neoplasm.[3]
- ***Angiosarcoma:*** The rare examples originating in brain or meninges.[3]
- ***Kaposi sarcoma:*** This malignant neoplasm is characterized by spindle-shaped cells lining or forming slit-like blood vessels and is only exceptionally encountered as a parenchymal or meningeal tumour in the setting of AIDS.[3]

Haemangiopericytoma:

- ***Definition:*** A highly cellular and vascularized mesenchymal tumour exhibiting a characteristic monotonous low-power appearance and a well-developed, variably thick-walled, branching "staghorn" vasculature; almost always attached to the dura and having a high tendency to recur and to metastasize outside the CNS.[3]

- ***ICD-O codes:*** Haemangiopericytoma 9150/1. Anaplastic haemangiopericytoma 9150/3.[3]
- ***Grading:*** Haemangiopericytomas correspond histologically to WHO grade II, with anaplastic haemangiopericytomas corresponding to WHO grade Ill.[3]
- ***Localization:*** Primary haemangiopericytomas of the CNS are almost invariably solitary and attached to the cranial or spinal dura.[3]
- ***Clinical features:*** As suggested by their location, the symptoms of meningeal haemangiopericytoma are indistinguishable from those of meningioma.[3]
- ***Neuroimaging:*** On plain films, a well-demarcated, lytic-lesion of adjacent bone supports haemangiopericytoma, whereas hyperostosis, a typical feature of meningioma is absent.[3]
- ***Macroscopy:*** At surgery, meningeal haemangiopericytoma is a solid, well-demarcated tumour. It has a tendency to bleed during removal, sometimes profusely.[3]
- ***Histopathology:*** Haemangiopericytomas are monomorphous tumours tumours composed of closely peaked, randomly oriented tumour cells with little intervening fibrosis. Cytoplasm is scant and cell borders are indistinct. Nuclei are round to oval, occasionally elongated, with

moderately dense chromatin and inconspicuous nucleoli, lacking the pseudo-inclusions characteristic of meningiomas.[3]

- ***Immunohistochemistry:*** Haemangiopericytoma cells are diffusely immunoreactive for vimentin ‘(85%), factor Xllla (80-100%) in individual scattered cells.[3]

Melanocytic lesions:

- ***Definition:*** Primary melanocytic neoplasms of the CNS that arise leptomeningeal melanocytes and that can be diffuse or circumscribed, benign or malignant. This group includes (1) diffuse melanocytosis and melanomatosis, (2) melanocytoma and (3) malignant melanoma.[3]
- ***Incidence:*** Melanocytoma account for 0.06 – 0.1% of brain tumours.[3]
- ***Neuroimaging:*** CT and MRI of melanocytosis and melanomatosis shows diffuse thickening and enhancement of the leptomeninges, often with focal nodularity.[3]
- ***Histopathology:*** Diagnosis hinges on the recognition of tumour cells that have melanocytic differentiation. Most benign and malignant melanocytic lesions display melanin pigment finely distributed within tumour cells and coarsely distributed within the tumour stroma and the cytoplasm of tumoural macrophages (melanophages).[3]

Germ cell tumours:

CNS germ cell tumours:

- ***Definition:*** Morphological and immunophenotypic homologues of gonadal and other extraneuraxial germ cell tumours.
- ***ICD-O codes*:**[3]

  - Germinoma (9064/3). - Teratoma (9080/1).
  - Mature teratoma (9080/0). - Immature teratoma (9080/3)
  - Teratoma with malignant transformation (9084/3).
  - Yolk sac tumour (9070/3). - Embryonal carcinoma (9070/3)
  - Choriocarcinoma (9100/3)

- ***Incidence:*** Geographic incidence varies considerably. Most prevalent in far-east Asia, CNS germ cell tumours accounted for 2-3% of primary intracranial neoplasms, and for 8-15% of specifically paediatric.[3]
- **Age and sex distribution:** Approximately 80-90% of CNS germ cell tumours afflict subjects younger than 25 years of age.[3]
- ***Localization:*** CNS variants preferentially affect the midline: 80% or more arise in structures about the third ventricle.
- Neuroimaging: The neuroradiological profiles of CNS germ cell tumours are largely non-specific and definitive histological subclassification requires tissue examination.[3]

- ***Germinoma:*** The pure germinoma, the most common CNS germ cell tumour, is populated by large cells that appear un differentiated and that resemble primordial germinal elements (of which, in theory, they represent the neoplastic counterparts).[3]
- ***Teratoma:*** Teratomas differentiate along ectodermal, endodermal and mesodermal lines (e.g. they recapitulate somatic development from the three embryonic germ layers). Mature and immature variants require distinvtion.[3]
- ***Mature teratoma:*** Mature teratomas are composed exclusively of fully differentiated, adult-type tissue elements. Mitotic activity is low or absent. The more common ectodermal components encountered in such tumours include skin, brain and choroid plexus. Mesodermal representatives include cartilage, bone, fat and muscle (both striated). Cysts lined by epithelial of respiratory or enteric type are the useful endodermal participants, with some examples also containing pancreatic or hepatic tissue. Not infrequently, gut-like structures are formed, replete with mucosa and muscular coats.[3]
- ***Immature teratoma:*** This teratoma variant contains incompletely differentiated components resembling foetal tissues. Such incompletely differentiated areas mandate classification of the lesion as an immature teratoma even if they constitute only minor elements in an otherwise differentiated tumour, Particularly common are a hypercellular and

mitotically active “stroma” reminiscent of embryonic mesenchyme and primitive neuroectodermal elements that may fashion neuroepithelial rosettes and canalicular arrays mimicking the developing neural tube.[3]

- ***Teratoma with malignant transformation:*** These are generic designations for the occasional teratomatous neoplasm that contains as an additional malignant component a cancer of conventional somatic type.[3]
- ***Yolk sac tumour:*** This neoplasm is composed of primitive- appearing epithelial cells-putatively representing yolk sac endoderm-set in a loose, variably cellular and often conspicuously myxoid matrix resembling extra-embryonic mesoblast.[3]
- ***Embryonal carcinoma:*** The embryonal carcinoma is composed of large cells that proliferate in cohesive nests and sheets, form abortive papillae of line irregular, gland-like spaces.[3]
- ***Choriocarcinoma:*** The choriocarcinoma is characterized by extra-embryonic differentiation along trophoblastic lines. The diagnosis requires the identitication of cytotrophoblastic elements as well as syncytiotrophoblastic giant cell.[3]

Tumours of sellar region:

Craniopharyngioma:

- ***Definition:*** **A** benign, partly cystic epithelial tumour of the sellar region presumably derived from Rathke pouch epithelium.
- ***ICD-O codes:***
  - Craniopharyngioma (9350/1)
  - Adamantinomatous craniopharyngioma (9351/1).
  - Papillary craniopharyngioma (9352/1).
- ***Grading:*** Craniopharyngiomas correspond histologically to WHO grade I.
- ***Incidence:*** Craniopharyngiomas account for 1.2-4.6% of all intracranial tumours, corresponding to 0.5-2.5 new cases per million population per year, being more frequent in Nigerian (18% of all CNS tumours).[3]
- ***Localization*****:** The most common site is suprasellar with a minor intrasellar component. Unusual locations such as sphenoid sinus have been reported.[3]
- **Clinical features:**
  - *Symptoms and signs:* Clinical features are non-specific and essentially include visual disturbances (observed in 62-84% of the patients, more frequently in adults than in children) and endocrine deficiencies (observed in 52-87% of patients, more frequently in children).[3]

- ***Neuroimaging:*** for adamantinomatous craniopharyngioma, radiography provides an accurate depiction of the configuration of the sella and the typical calcifications CTs show contrast enhancement of the solid portions and the cyst capsule, as well as the typical calcifications.[3]
- ***Macroscopy:*** Typically a lobulated solid mass, on closer inspection, adamantinomatous craniopharyngiomas often demonstrate a spongy quality as a result of a variable cystic component.[3]
- ***Histopathology:*** Adamantinomatous craniopharyngioma is recognized by the presence of squamous epithelium disposed in cords, lobules and irregular trabeculae bordered by palisaded columnar epithelium. These islands of densely packed cells merge with loosely cohesive aggregates of squamous cells known as stellate reliculum. Nodules of “wet keratin” representing remnants of pale nuclei embedded within an eosinophilic keratinous mass are found in either the compact or looser areas. Cystic cavities containing squamous debris are lined by flattened epithelium. Granulomatous inflammation associated with cholesterol clefts and giant cells may be seen, but this is more typical of the xanthogranuloma.[3]

Granular cell tumour of the neurohypophysis:

- ***Definition:*** An intrasellar and/or suprasellar mass arising from the neurohypophysisor infundibulum, composed of nests of large cells with

granular, eosinophilic cytoplasm due to abundant intracytopiasmic lysosomes.[3]

- ***ICD*-O code:** 9582/0.
- ***Grading:*** Granular cell tumours correspond to WHO grade I.
- ***Localization:*** GCTs arise along the anatomic distribution of the neurohypophysis, including the posterior pituitary and pituitary stalk/infundibulum.[3]
- ***Clinical features:***

Symptoms and signs: The most common presenting symptom is visual field deficit secondary to compression of the optic chiasm.[3]

- ***Neuroimaging:*** MRI typically shows a well-circumscribed suprasellar mass that most frequently displays homogeneous or heterogeneous contrast enhancement.
- ***Histopathology:*** GCTs consist of densely packed polygonal cells with abundant granular eosinophilic cytoplasm. The architecture is typically nodular.
- ***Immunohistochemistry:*** GCTs are variably positive for CD68(KP1)S-100.

Metastatic tumours of the CNS:

- ***Definition:*** Tumours that originate outside the CNS and spread secondarily to the CNS via the haematogenous route (metastasis) or by direct invasion from adjacent tissues.[3]

OBJECTIVES

General objective:

To determine the histopathological pattern of brain tumors among Sudanese patients operated in Alshaab Teaching Hospital from January 1st 2009 to 1st April 2010.

Specific Objectives:

1. To determine the prevalence of brain tumors among Sudanese patients diagnosed and operated at Alshhaab Teaching Hospital .

2.To determine the age, sex, residence in the mentioned group.

2. METHODOLOGY

2.1. Study Design:

This is descriptive retrospective study.

2.2. Study period: From 1/1/2009 to 1/4/2010.

2.3. Study field:

The study was carried out at the National Health Laboratory and Alzhrawi Laboratory (Khartoum).

The National Health Laboratory (NHL) is a National reference laboratory located in the center of Khartoum; it has several pathologic departments including a Histopathology Department and Cancer Research Center of Sudan. NHL is guided by a professional cadre and receives samples from different parts of Sudan.

Alzhrawi Laboratory (private lab).

2.4. Study Population:

All cases of brain tumours that presented to NHL and Alzhrawi Laboratory in the period of the study.

2.4.1. Inclusion criteria:

All cases of brain tumours that were diagnosed histopathologically at the two mentioned centers .

2.4.2. Exclusion Criteria:

- Brain tumours cases that had no histopathological slides in the histopathology laboratory mentioned centers.

- Any case with inadequate information.
- Poorly stained slides.

2.5. Sampling technique:

2.5.1. Ethical consideration:

Consent was taken from the General Directors of National Health Laboratory and Alzahrawi Laboratory.

2.5.2. Data collection:

Data were collected from patient's request forms in a pre designed questionnaire (appendix). All the histopathological slides of the study were retrieved and reviewed with the help and supervision of experienced histopathologists to confirm the brain neoplasm diagnosis, determine the histopathological types of the tumors and classify the tumor using WHO grading system.Eighty cases from Alzahrawi and (10) cases from National Health Lab.

2.6. Data processing and analysis:

The data were electronically processed and analyzed by computer using Statistical Package for Social Sciences (SPSS) software. The obtained results presented in tables and figure.

RESULTS

The number of patients included in the study was 90 patients, who are diagnosed as brain tumour in 14 months period from January 2009 to April 2010.

Characteristics of the study population are as follows:

Age distribution:

The minimum age affected by brain tumours was 2 year, and the maximum was 80 years with a mean age group affected by brain tumours was 45 to <60 years showing the highest percentage of brain tumors 28 cases (30.9%) followed by the age 10 <20 10 years 16 cases (16.7%) and then the age 30 to <49 years 17 cases (18.8%). (Table No. 3).

Gender distribution:

Male patients constituted (58.8%) 53 cases compared to female (41.1%) 37 cases. With male to female ratio 1.43 : 1.

Distribution of patients according to residence:

Patients coming from centre of Sudan are 57 patients (63.3%), 6 patients (6.6%) from north Sudan, 3 patients (3.3%) from south Sudan and 3 patients from East Sudan (3.3%) (Figure 2).

Distribution of patients according to diagnosis: meningioma constituted 48 cases (53.3%), this was followed by a strocytoma 16 cases (17.7%), pituitary a denoma 8 cases (8.8%), craniopharyngioma 6 cases (6.6%), ependymoma 4 cases (4.4%), oligodendroglioma 3 cases (3.3%),

medulloblastoma 3 cases (3.3%), epidermoid cyst 1 case (1.1%) and undiagnosed 1 case (1.1%). (Table No. 1).

Clinical Presentation:

Headache was the commonest presenting syptom in 61,1% of patients, this is followed by convulsions (40%), blurring of vision (15.5%), loss of smell (11.1%), change of mood (10%), milky breast secretion (6.6%), unsteady gait (5.5%). (Table No. 4).

Duration of the illness:

The duration of syptoms, until the patients sought medical advice, ranged from 1 month to greater than 2 years. Four to seven months duration is the most frequent time interval taken by the patient, accounting (28%) of patients (Figure No. 3).

WHO staging of patients:

The study showed that the percentage of WHO grade I among the tumours patients was (74.4%), WHO grade II (11.1%), WHO grade III (4.4%) and WHO grade IV (7.7%) (Figure No. 1).

Histological sub-types of meningioma:

The most common sub-type of meningioma was mixed type (41%), this followed by meningothelial (35.4%).

Atypical (8.3%), fibrous (6.3%) psammomatous (4.2%) and anaplastic (4.2%). (Table No. 7).

Histological sub type of astrocytoma:

The most frequent sub type of astrocytoma was pilocytic astrocytoma (62.1%) followed by glioblastoma (31.2%) and fibrillary astrocytoma (6.2%) (Table No. (8).

Distribution of brain tumors according to Radiological finding:

- Ninety five percent of meingioma in MRI was solid, while (5%) showed cystic degeneration.
- Astroctyoma (55.8%) was solid, while (44.2%) cystic.
- Caniopharyngioma: all the cases were solid. (Table No. 6).

Refere to table No. (9) Location of brain tumour:

We find that meningioma commonly in the parietal labes; this is followed by frontal, temporal, occipital.

Supra sellar, olfactory groove, orbital and then cerebellum. Astrocytoma commonly in the parietal lobes followed by cerebellum, temporal lobes and suprasellar.Ependyrmoma in the frontal lobe. Oligodendroglioma in the temporal then frontal and occipital. Pituitary ademoma, all the cases were supra sellar. Craniopharyngioma more supraseller followed by frontal lobes.

Medullo blastoma, the commonest site is the frontal labes.

Refer to table No. 5, 48 cases in the cerebrum of the brain, 30 cases in the left side and 18 cases in the right side.

Table No. (1) Distribution of the patient who attended to NHL and Alzahrawi labs according to Diagnosis of brain tumour.

	Frequency	Percentage
Meningioma	48	53.3%
Astrocytoma	16	17.7%
Ependymoma	4	4.4%
Oligo dendroglioma	3	3.3%
Pituitary adenoma	8	8.8%
Craniopharyngioma	6	6.6%
Medulloblastoma	3	3.3%
Epidermoid cyst	1	1.1%
Undiagnosed	1	1.1%
Total	**90**	**100%**

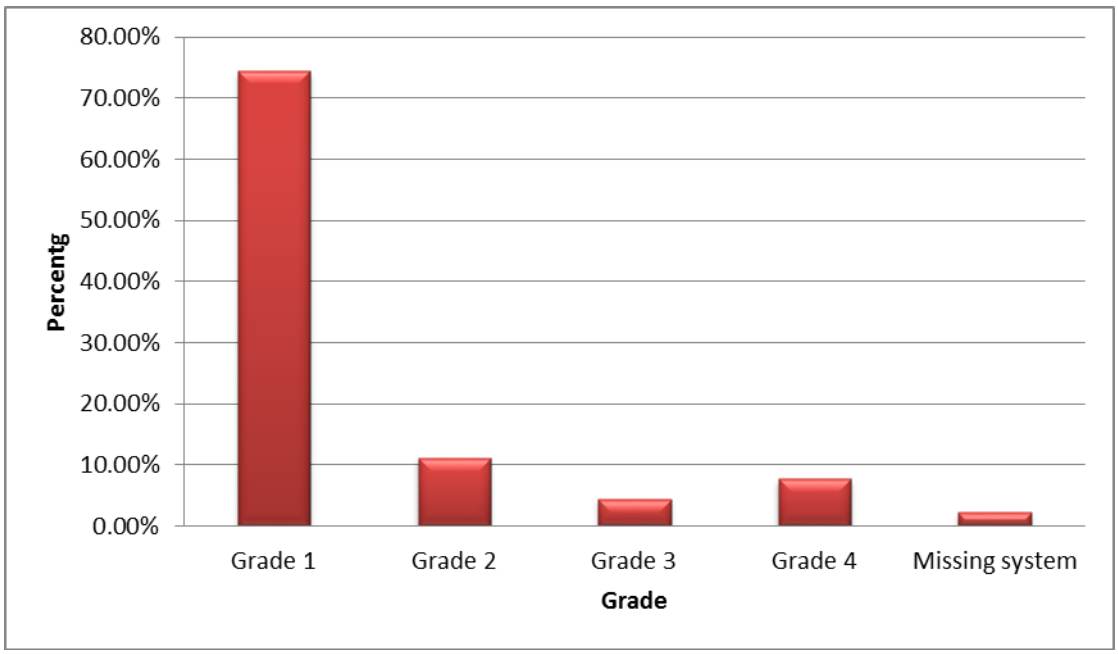


Figure (1) Distribution of the patient diagnosis who attended to NHL and Alzahrawi labs according to WHO Grading of brain tumours

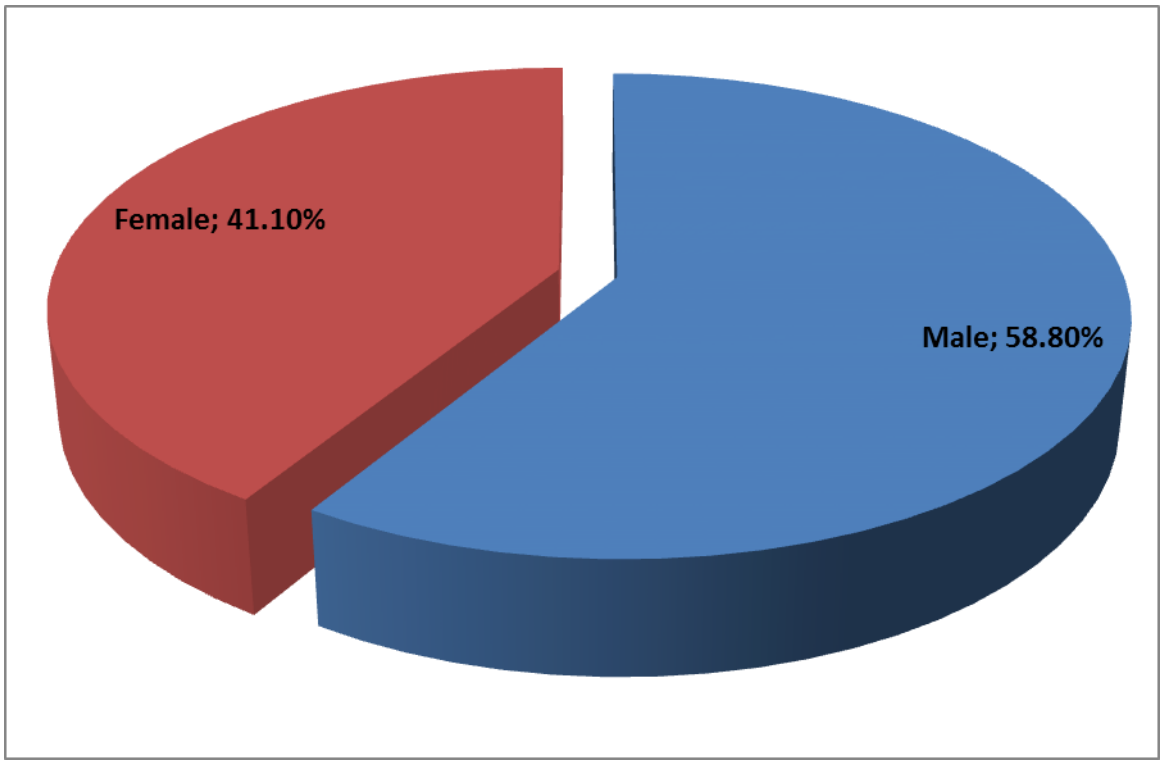


Figure (2): Distribution of the patient of brain tumours who attended to NHL and Alzahrawi labs according to Gender with male to female rashio 1,43:1

Table No. (2) Distribution of the patient of brain tumours who attended to NHL and Alzahrawi labs according to Residence

Residence	Frequency	Percentage
North	6	6.6%
West	21	23.3%
East	3	3.3%
South	3	3.3%
Center	57	63.3%
Total	**90**	**100%**

Table No. (3) Distribution of the patient of brain tumours who attended to NHL and Alzahrawi labs according to Age Group

	Frequency	Percentage
Less than 4 years	4	4.4%
5-9	2	2.2%
10-14	6	6.6%
15-19	10	11.1%
29-24	3	3.3%
25-29	2	2.2%
30-34	6	6.6%
35-39	11	12.2%
40-44	13	14.4%
45-49	7	7.7%
50-59	8	8.8%
60-64	3	3.3%
65-69	3	3.3%
70-74	2	2.2%
Higher than 75	1	1.1%
Unavailable	2	2.2%
Total	**90**	**100%**

Table No. (4) Distribution of the patient of brain tumours who attended to NHL and Alzahrawi labs according to Clinical Presentation.

Clinical presentation	Frequency	Percentage
Headache	55	61.1%
Convulsion	36	40%
Blurring of vision	14	15.5%
Loss of smell	10	11.1%
Change of mood	9	10%
Milky breast secretion	6	6.6%
Hemiplegia	5	5.5%
Unsteady gait	5	5.5%
Growth Retardation	4	4.4%
Dizziness	3	3.3%
Others	7	7.7%

Table No. (5) Others clinical presentation among patients of brain tumour in NHL and Alzahrawi Laboratory.

Clinical presentation	Frequency	Percentage
Decrease hearing	1	1.1%
Difficulty in walking	1	1.1%
Drowsiness	2	2.2%
Fatiquability	1	1.1%
Loss of vision	1	1.1%
Slurred speech	1	1.1%

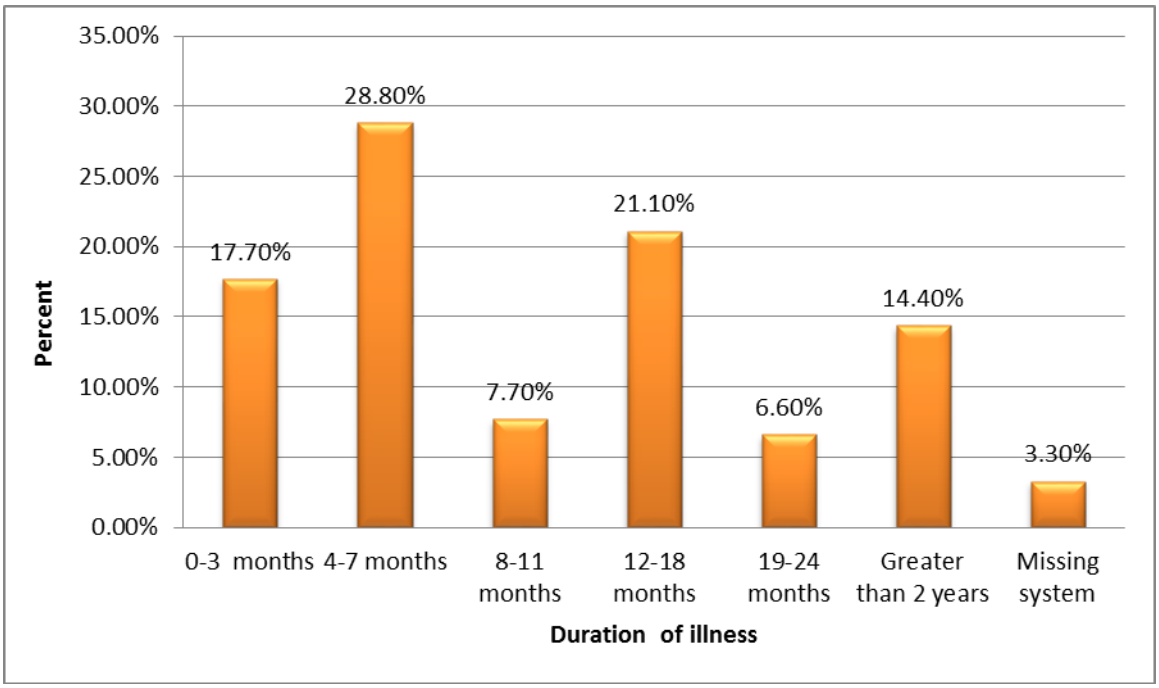


Figure (3) Distribution of the patient of brain tumours who attended to NHL and Alzahrawi labs according to duration of the illness.

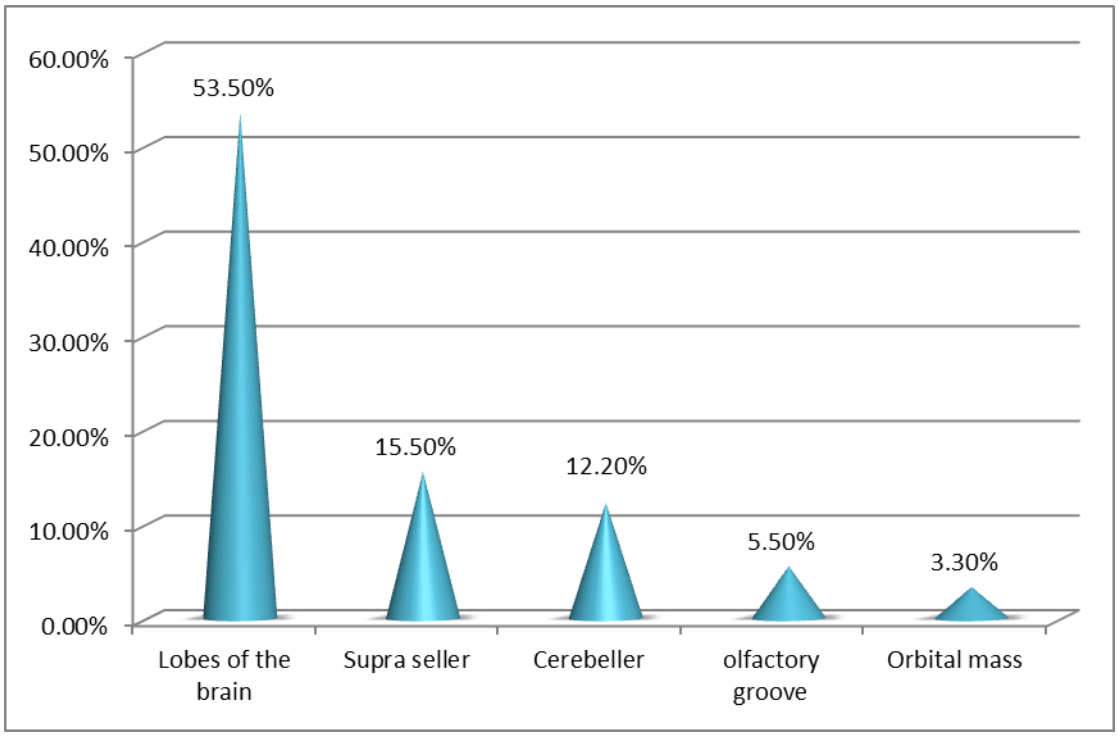


Figure (4) Brain tumour anatomical site among the study population

Table No. (6) Distribution of the brain tumour according to the side of cereberum of the brain.

Left	Right
30	18

Table No. (7) Distribution of brain tumour acceording to consistency of the tumour being solid or cystic .

	Solid	Cystic
Meningioma	45	3
Astrocytoma	7	9
Ependymoma	3	1
Oligo dendroglioma	1	2
Pituitary ademoma	8	1
Crainiopharyngioma	5	-
Medulloblastoma	3	1
Epidermoidcyst	-	1
Undiagnosed	1	-

Table No (8) Distribution of the meningioma according to the subtypes

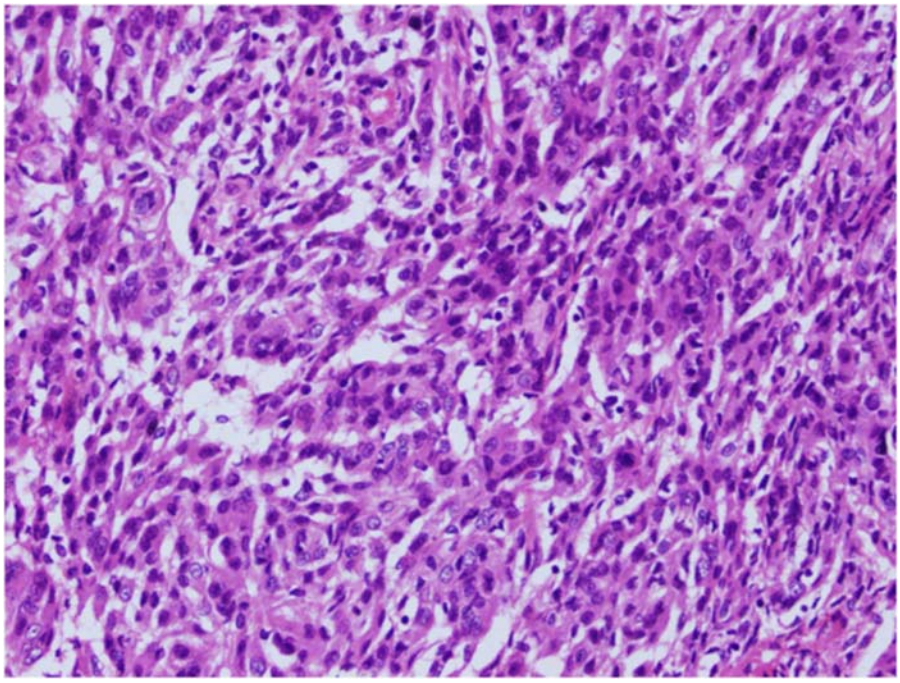
	Frequency	Percentage
Meningothelial	17	35.4%
Fibrous	3	6.3%
Mixed type	20	41.7%
Psamommtous	2	4.3%
Atypical	4	8.3%
Anaplastic	2	4.2%
Total	**48**	**100%**

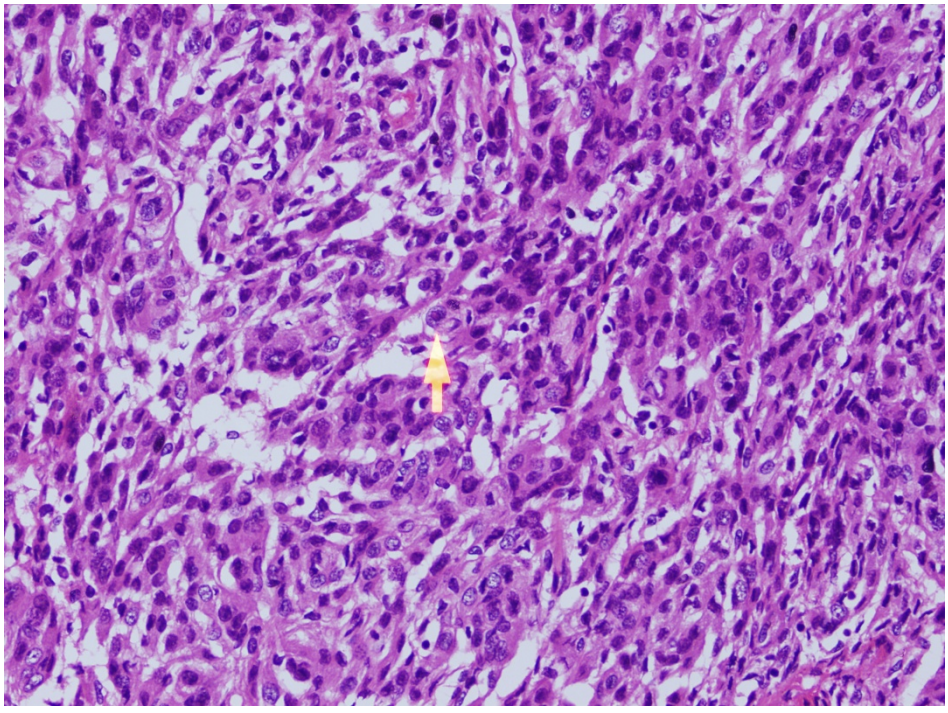
Table No. (9) Distribution of astrocytoma according to sub-types

	Frequency	Percentage
Pilocytic astrocytoma	10	62.1%
Fibrillary	1	6.2%
Glioblastoma	5	31.2%
Total	**16**	**100%**

Table No. (10): Distribution of brain tumours patients according to site in different areas of the brain

Diagnosis	Parietal lobes	Temporal	Frontal	Occipital	Cerebellar	Supra seller	Olfactory groove	Orbital mass
Meningioma	**13**	**5**	**9**	**5**	**3**	**5**	**5**	**3**
Astrocytoma	**6**	**3**	**-**	**2**	**5**	**2**		
Ependymoma			**3**					
Oligodendroglioma	**1**	**1**	**1**	**1**				
Pituitary adenoma								
Cranio-pharyngioma		**1**	**2**			**8**		
Medulloblastoma				**1**		**5**		
Epidermoid cyst			**1**					
Undiagnosed			**1**					





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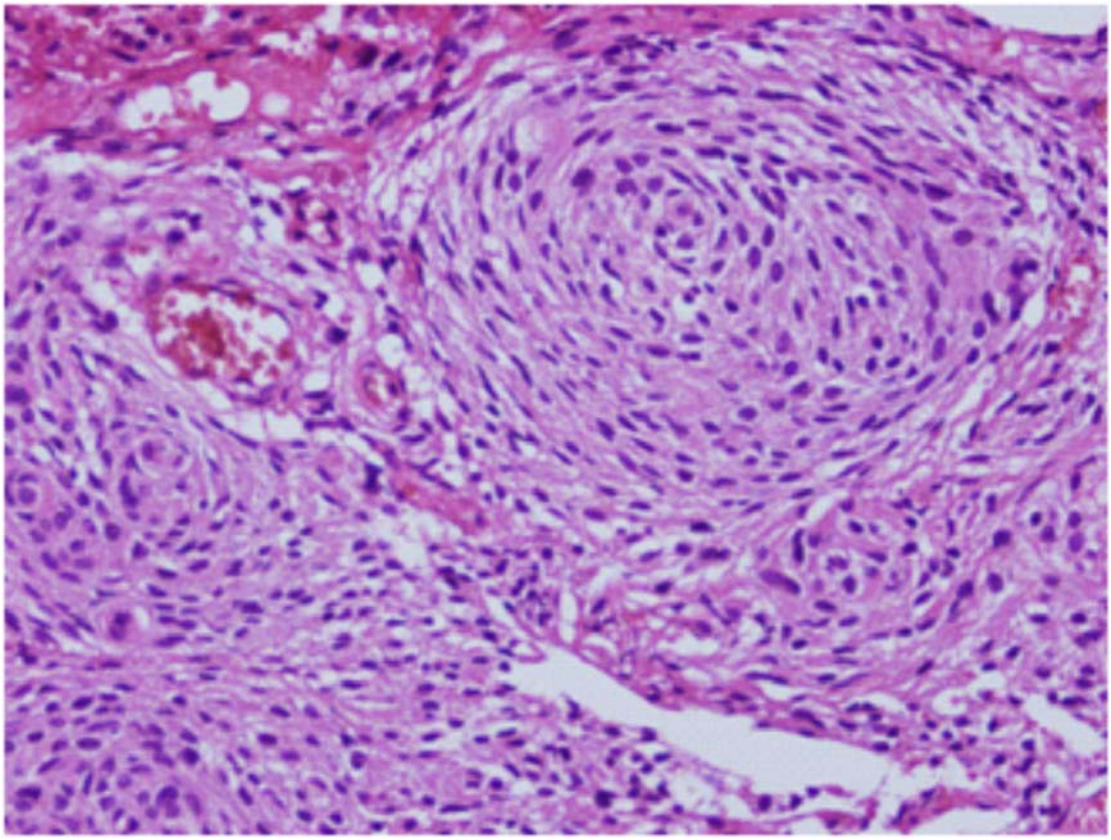

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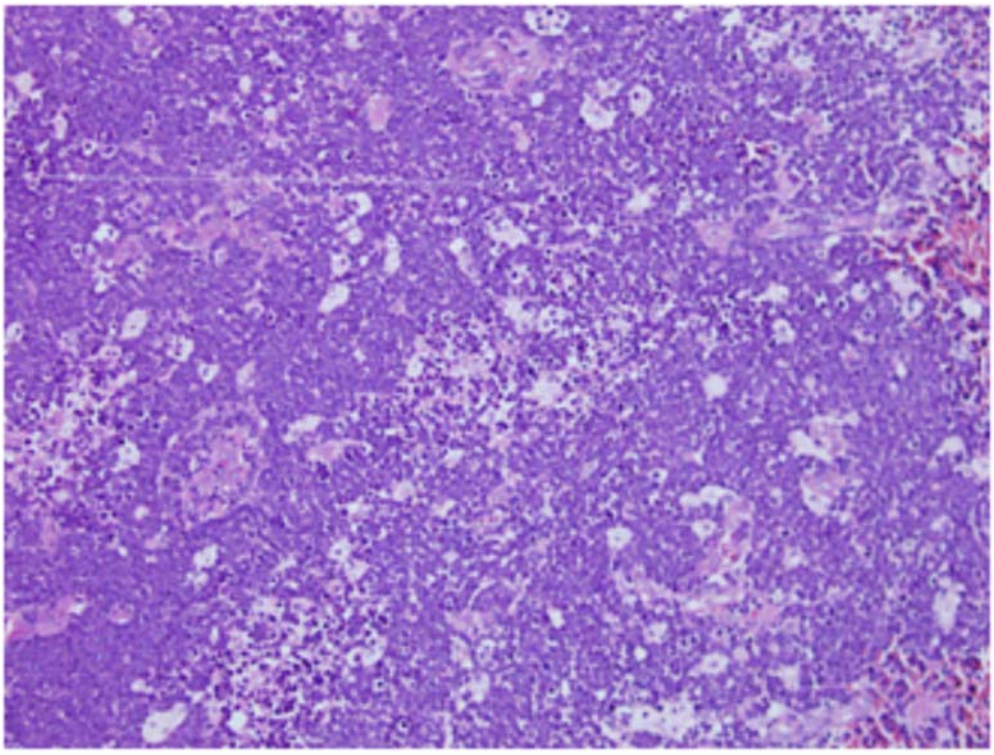

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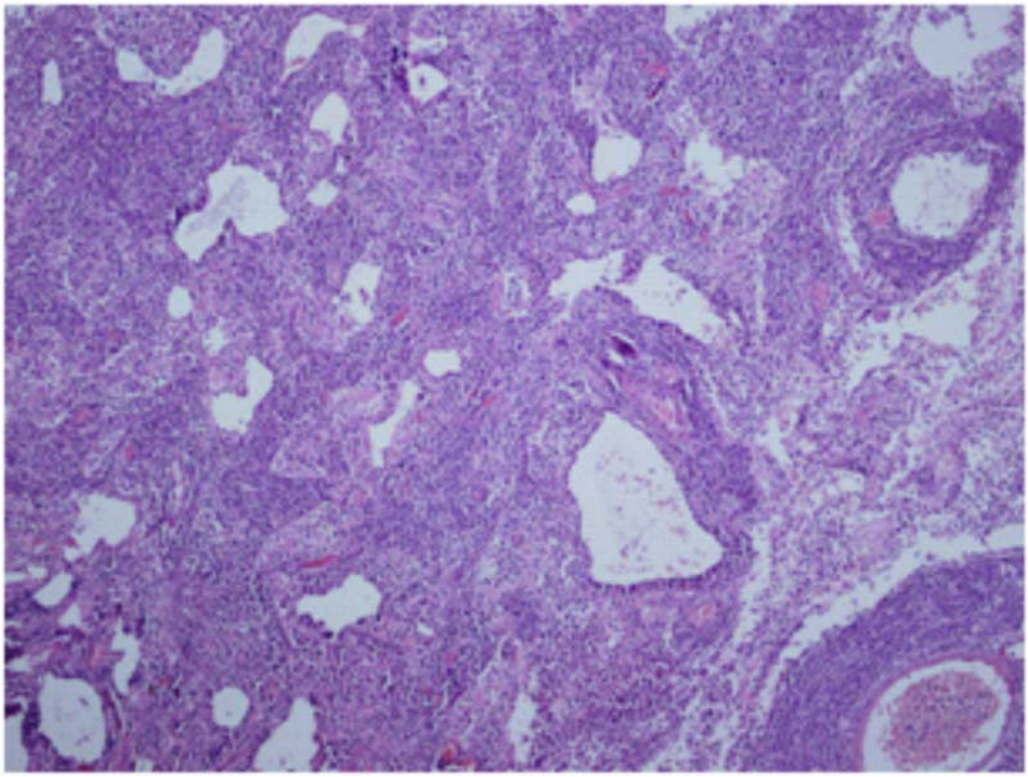

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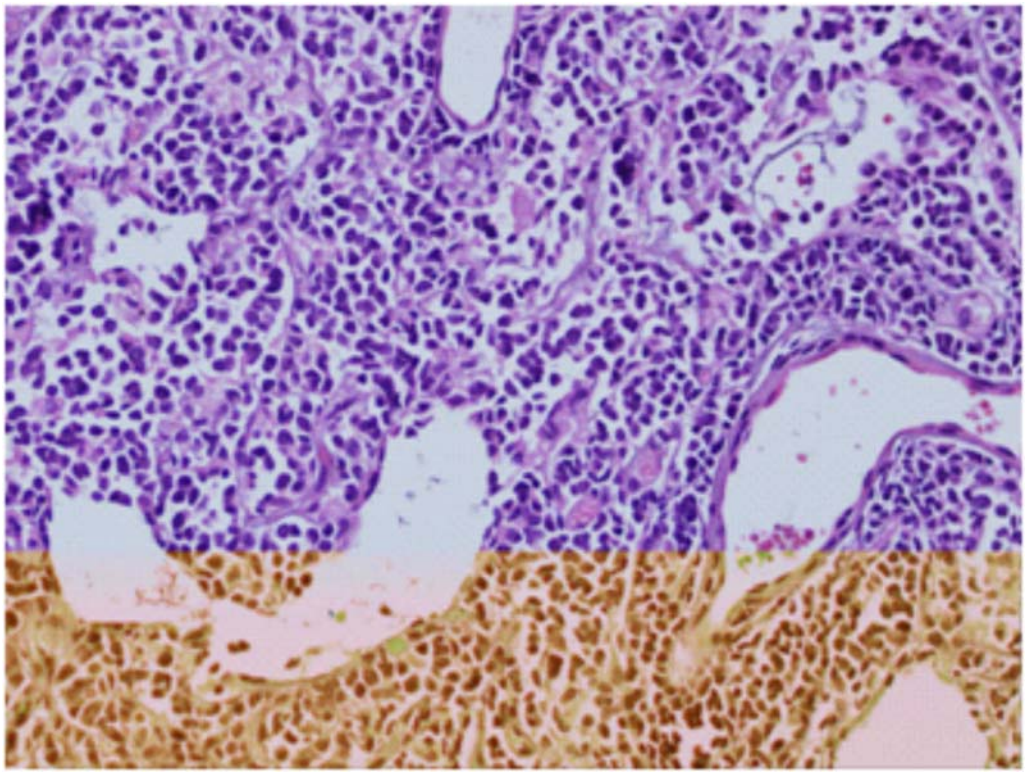

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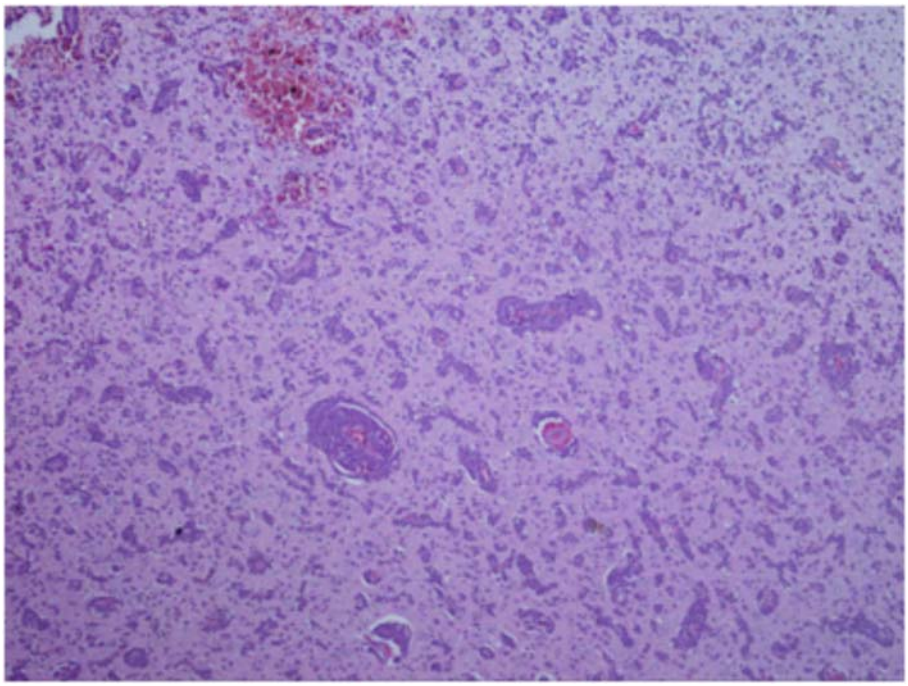

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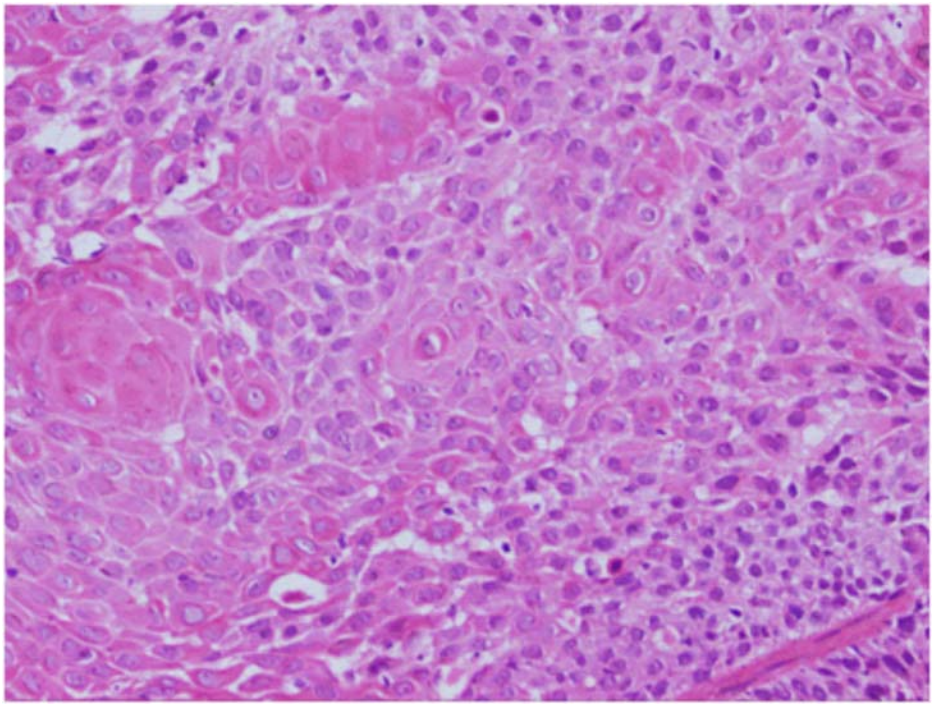

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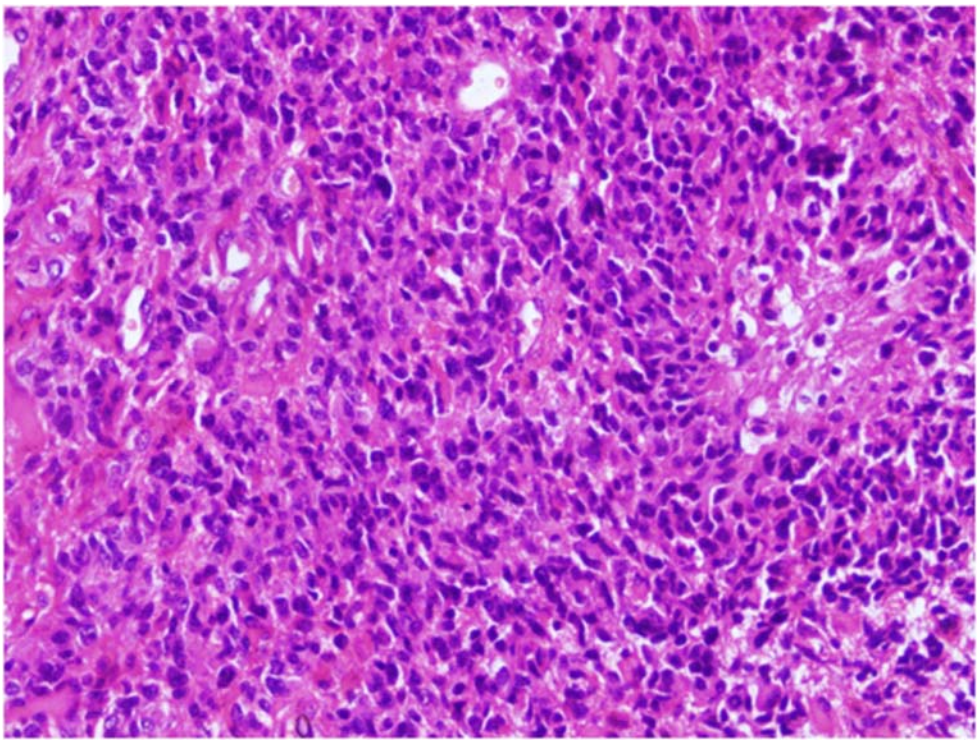

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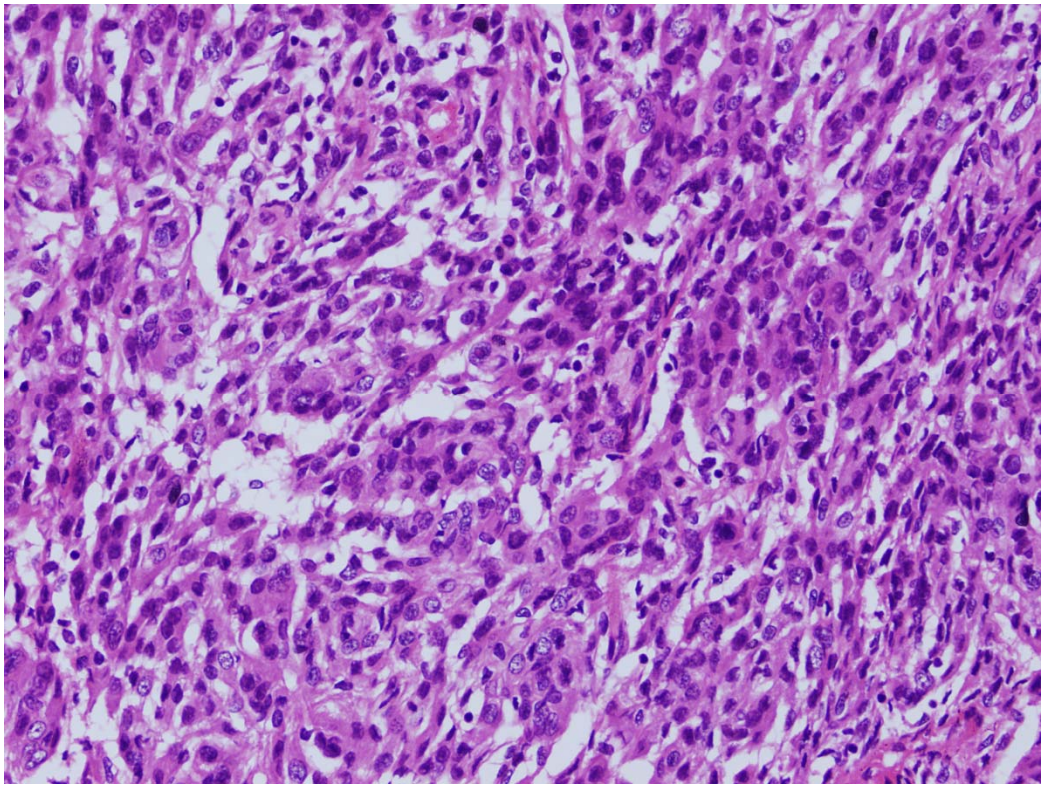
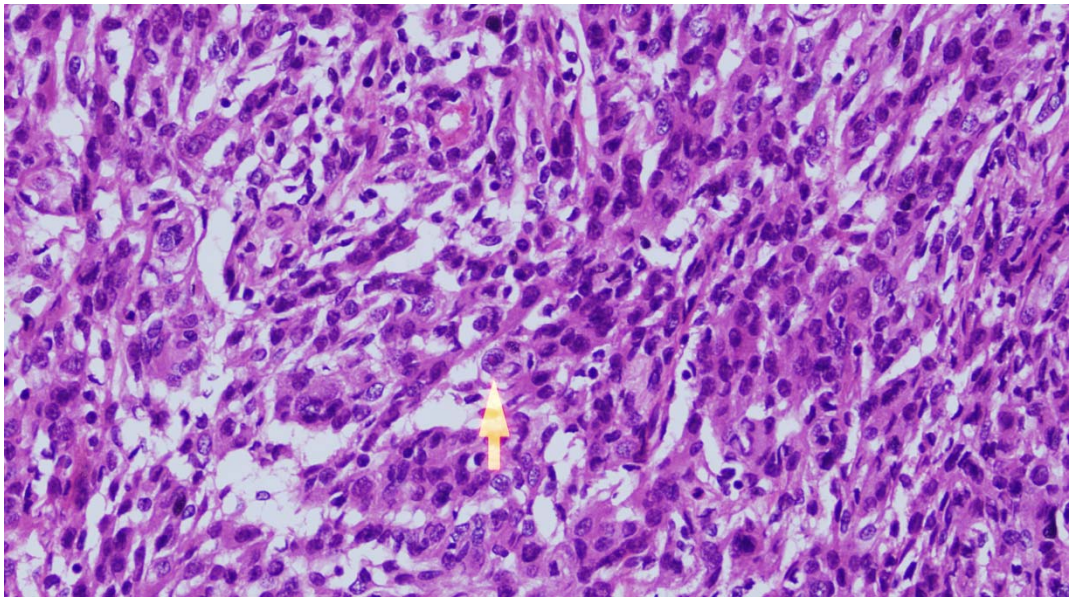


38 10 MENGIOMA GRADE 2 NUCLEOLI



38 10 MENINGIOMA G2 X40 NUCLEOLI

DISCUSSION

Brain tumours are common, the annual incidence rate appears to increase steadily with age. Literature review showed no previous histopathological studies concerning brain tumours were carried out in Sudan. So, this is the first histopathological study of general pattern of brain tumours in Sudan.

It may not be the exact in incidence because many cases were diagnosed in private laboratories and other hospital laboratories that were not included in this study. The actual number of brain cancers is most probably higher, but since the two selected institutions are the main histropathology centers in Sudan that received brain tumours samples, we can considered these results are acceptable. In Sudan as in most developing countries, at present there is no reliable statistical information. The poor registration of medical data was one of the biggest obstacles for this study. It made the data interpretation and statistical analysis difficult.

The mean age at presentation in this study is 45 years, maximum was 80 years and the minimum age is 2 years. This correlates well with a WHO data.[3] Also in a study by Middle East Concerum Centre,[1] that brain tumours can occur at any age.

Our study showed that there is association between the age and the diagnosis, that 19 (cases) out of (48) cases of meningioma is between the age of 40-49 with 1 case at the age of 5-9 years and 1 case higher than 75

years. Within the following age groups the most common primary brain tumours are:

- In ages 0-4, medulloblastoma, pilocytic a strocytoma, craniopharyngioma, Ependymoma.
- In ages 5-9, medulloblastoma.
- In age 10-14, pilocytic astrocytoma followed by craniophryngioma and medullobastoma.
- In age 15-19, pilocytic astrocytoma, followed by craniopharyngioma and glioblastoma.
- In age 20 – 24, pilocytic strocytoma,
- In age 25 – 29, meningioma followed by pituitary adenoma.
- In age 30 – 34 meningioma.
- In age 35 – 39 meningioma followed by pilocytic astrocytoma.
- In age 40 – 49 meningioma.
- In age 50 – 54 meningioma.
- In age 55 – 59, pituitary adenoma followed by meningioma.

This results are similar to the results reported by American Brain Tumour Association excepted of age of 15-19, the commonest brain tumour was pituitary adenoma and also in age of 20 – 34, pituitary adenoma.[5]

Also this results are consistent with the WHO data that meningioma common in adult while pilpcytic astrocytoma, medulloblastoma, and craniophryngioma in children.[3]

Also M, William Schwartz said that astrocytoma constituted 75% of childhood CNS tumours followed by medulloblastoma 20%, ependymoma and craniopharyngioma.[70]

Male to female ration in this study is 1.43 : 1 with a male predominant this correlate with MECC studies (1) and with study done in Alsabah-hospital in Kuwit.[73] So brain tumour is more common in male than female.

Our study found that the most common brain tumour is meningioma (53.3%) this correlate with the Dr. Hussein Abu-Salih study which done in Alshaab Teaching Hospital over a 10 years period (1971-1981).[75] One hundred twenty three cases of brain tumour encountered in the study. Meningioma constituted (45.5%).[75] Also correlate with Dr. Arbab study which done in Alshaab Teaching Hospital in a period of May 2005 – December 2007. They found that meningioma was the most common brain tumour constituted 72% followed by astrocytoma 22%.[74] Also correlate with study done in Al-sabah Hospital, Kuwait between 1995 and 2009, they found that the most common brain tumour was meningioma (28%), this followed by pituitary adenoma 19%,

glioblastoma (15%), a strocytoma (13%.).[73] In childhood astrocytoma (35.34%) followed by medulloblastoma (22.56%).[73]

But is not correlate with study done in Howard University and DC General Hospital, 1954 to 1973, they found that the most common brain tumour in black was metastatic tumour constituted 34%, this is followed by glioma 28%, meningioma 20%, pituitary a denoma 13,1%.[72] Also not correlate with (1) the MECC (Middle East Concerum Centre) and with Saint John/s Health Center[71] studies, they said that the most common brain tumour is glioma. So why we have high incidence of meningioma? This may need more studies about the causes of brain tumours and about the risk factors and molecular.

The study showed that the percentage of WHO grade 1 among brain tumour was (74.4%). Grade 1 meningioma constituted (87.9%). With 4.1% grade IV

This finding in correlate with the Saint John's Health Center studies.[71]

Regarding meningiom's sub types, we found that the most common subtype of meningioma was mixed type (41%). This result is not consistent with the Dr. Muna's study in meningioma who said that the common sub type is meningothelial? Also not consistent with the WHO which stated that the most common is meningothelial menigioma.[3]

In our study we found that meningioma common in the cerebrum, this followed by supra sellar, olfactory groove, orbital, cerebellum.

These results were consistent with WHO data.[3] Also astrocytoma commonly in the parietal lobes followed by cerebellum, this is correlate with the WHO, who stated that pilocytic astrocytoma is common in the cerebellum in the children,[3] ependymoma in the frontal lobe, this not go the literature because ependymoma is common in the ventricles.

Regarding residence (63.3%) from the centre of Sudan. (33.3%) from the East. So it constituted a high percentage from the total in our study, we don't know the causes. It needs further studies.

Regarding the risk factors, it is not a heritable condition, but associated with several familial syndromes, like neuro fibromatosis, with gliomas and meningioma. Tuberous sclerosis with gliomas and rarely ependymomas, li fraumani syndrome with astrocytoma.[70] But in Sudan there is no studies.

Regarding the clinical presentation, the most common presenting syptom is headache followed by convulsion and blurring of vision as theses syptoms of increase intra cranial pressure-ataxia was a syptom of cerebellum lesion, so our clinical presentations correlated with the final diagnosis.

There are one case which was not diagnosed in spite of panel of immuno histochemistry that LCA negative and CD 117 positive.

CONCLUSION

The study concluded that, meningioma was found to be the commonest brain tumour among the study population, followed by astrocytoma, then pituitary adenoma and craniopharyngioma. Also, it was found that, it was more frequent among males than females as well as it is more common in the center of Sudan followed by the West, then the North. The most presenting symptoms were headache and convulsions. Brain tumours were more common in the left than the right.. Benign tumours are more than the malignant.

RECOMMENDATIONS

- The study recommended for further studies, considering coverage of wider population and studying the risk factors.
- A full history of suspected patients should be obtained so as to explore all aspects of the disease.
- Health providers should organize specialized strategic program from brain tumour, and it is preferred to produce good efforts in its fund raising.
- Regarding patients, awareness should be raised for early detection of the disease.
- Good registrations of the clinical informations.

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بسم الله الرحمن الرحيم

University of Khartoum

The Graduate College
Medical and Health Studies Board

Questionnaire

Pattern of brain tumours in Sudanese Patients

Serial No: .....

1. **Gender:** 1.1. Male 1.2. Female ☐
2. **Age:** .....
3. **Residence:** 2.1. Khartoum 2.2. Dar Four 2.3. Kordofan
   2.4. Algezira 2.5. Others ..... ☐
4. **Tribe:** .....
5. **Clinical presentation:**
   5.1. Headache 5.2. Convulsion 5.3. Blurring of vision
   5.4. Change of mode 5.5. Dizziness 5.6. Unsteady gaits
   5.5. Others ..... ☐
6. **Duration:** .....
7. **Imaging MRI:**
   7.1. Parietal space occupying lesion: 1. Left ☐ 2. Right ☐
   a. Solid ☐ b. Cystic ☐
   7.2. Temporal: 1. Left ☐ 2. Right ☐
   a. Solid ☐ b. Cystic ☐
   7.3. Frontal: 1. Solid ☐ 2. Cystic ☐
   7.4. Occipital: 1. Solid ☐ 2. Cystic ☐
   7.5. Cerebellar: 1. Solid ☐ 2. Cystic ☐
   7.6. Supra sellar: 1. Solid ☐ 2. Cystic ☐
   7.7. Others .....

8. Diagnosis:

8.1. Meningioma	☐	8.2. Pilocytic astrocytoma	☐
8.3. Ependymoma	☐	8.4. Glioblastoma multiforme	☐
8.4. Oligodendroglioma	☐	8.5. Pituitary adenoma	☐
8.6. Crianio pharyngioma	☐	8.7. Medulloblastoma	☐
8.8. Metastasis	☐	8.9. Others:.....	

9. WHO grading:

9.1. I ☐ 9.2. II ☐ 9.3. III ☐ 9.4. IV ☐

10. Immuno-histochemistry: 10.1 Yes ☐ 10.2 No ☐

If "Yes" Specify: .....

11. Recurrent: 11.1 Yes ☐ 11.2 No ☐

Chapter One

Introduction, Literature review
and
Objectives

Chapter Two

Methodology

Chapter Three

Results

Chapter Four

Discussion, Conclusion
and
Recommendations

Appendix

References